TEXT BOOK

OF

PHYSIOLOGY

BY

W. RUTHERFORD, M.D., F.R.S.

PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF EDINBURGH

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BY

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F.R.SS. L. AND E.

PROFESSOR OF THE INSTITUTES OF MEDICINE OR PHYSIOLOGY

IN THE UNIVERSITY OF EDINBURGH

WITH NUMEROUS ENGRAVINGS ON WOOD

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PREFACE.

SINCE Physiology rests on a tripod of anatomy, chemistry, and physics, it is necessary in discussing vital phenomena to constantly refer to these departments of science. In a work of this description it must, however, be assumed that the student already possesses a general acquaintance with them. But with regard to anatomy it is necessary, in explaining the plan of the following work, to state that anatomy and physiology are so closely intertwined, that it is scarcely possible, even if it were advisable, to entirely separate the tuition of the one from that of the other. In the early history of medical education anatomy and physiology were professed by the same teacher, who first described the form, structure, and relations of a part of the body, and then proceeded to elucidate its functions. The method was natural, and is still to some extent adhered to, although the extensive development of anatomy and physiology has rendered their division between two teachers necessary.

No countenance, however, is given in this book to the futile attempt which has now and then been made to limit the tuition of the anatomist merely to structure, and that of the physiologist merely to function; for such a division seriously damps the interest of the student, and interferes with that lucidity of exposition which a subject so important demands.

It is expedient for the physiologist to enter fully into the minute structure of the tissues and organs of the body. This subject is therefore included in the following work. On the other hand, the physiology of most of the joints, bones, ligaments, and muscles, is omitted; for that department of physiology is best professed by the anatomist.

I make a point of as far as possible explaining the experimental methods by which the more important physiological facts have been arrived at, because a bald statement of conclusions without an explanation of the experimental steps necessary for their attainment constitutes *cramming* as distinguished from *education*, and places the student in a helpless position when he is left to think and work for himself. To avoid this I enter into many experimental details which will appear tedious to superficial minds. I may therefore at once warn the *dilletante* that this book is not intended for any who are not resolved upon earnest study.

I long ago promised my students that I would write a text book, which would enable them more readily to follow my lectures. The serious labour in the preparation of woodcuts of histological subjects has been the principal cause of the delay in its appearance, for I am entirely of opinion that a text book of physiology requires copious illustration.

I have, as far as possible, repeated the observations of others, in order that I might be able to offer an opinion on disputed points.

I have to thank my former assistant Professor Stirling of Aberdeen for valuable suggestions, and my present assistant Dr. De Burgh Birch for some of the histological drawings.

It ought to be stated that the first hundred pages were printed off in October 1878.

UNIVERSITY OF EDINBURGH,
January 1880.

TEXT-BOOK OF PHYSIOLOGY.

SECTION I.

INTRODUCTION.

CHAPTER I.

HISTORICAL OUTLINE OF PHYSIOLOGY.

In Greece, some four and a half centuries before our era, Hippocrates first sought to establish medicine upon a rational foundation, and in so doing enunciated physiological theories, which, in some instances, long held sway over medical opinion. Long, however, before the time of Hippocrates hospitals for the sick had been built at the more celebrated medicinal springs of Greece. These Temples of Health were dedicated to a somewhat mythical individual named Æsculapius, and the priest-physicians, who ministered to the bodily as well as to the mental troubles of those who sought their aid, were termed *Asclepiadæ* or Æsculapians. Hippocrates was a priest-physician at one of these Æsculapian hospitals. Inheriting the medical traditions of a long line of ancestors, he, with a sagacity that proved him a fit contemporary of those who were raising Greece to the zenith of her fame, endeavoured to banish superstition from the art of medicine, and to render its practice *rational.* He ascribed all diseases to natural causes, and he counted it impiety to attribute one more than another to visitations from the gods. He strove, in a philosophical spirit, to accurately observe and record the facts of disease, and to found the art of medicine solely upon experience.

At that time it was fancied that matter consists of four elements—fire, air, earth, and water. Thales imagined that in *water* the secret of life may be found; Anaximines referred it to the *air;* Xenophon ascribed it to the *earth;* while Pythagoras and many of his followers maintained that *heat* is the cause of vital phenomena. Hippocrates agreed with Pythagoras in assigning an important place to the influence of heat, but he further maintained that there is a spiritual essence universally diffused, that constantly strives to preserve things in their normal condition, and to restore them to order when deranged. This principle he termed φύσις, or *Nature;* hence the term Physiology, derived from φύσις and λόγος. The term literally means Natural Philosophy; but it has long been employed to signify the *functions* of living things.

Hippocrates ascribed to this hypothetical entity, *Nature*, the power of selecting what is beneficial, and of rejecting what is detrimental to the body, and he moreover regarded it as a *vis medicatrix*, or healer of disease; notions which have held powerful sway until quite recent years.

After Hippocrates came Aristotle, who, amidst many other pursuits, was a zealous student of animal life. He may be regarded as the father of Natural History, on account of his numerous writings about animals, many of which he dissected in endeavouring to discover the uses of their parts; but although he proceeded by the method of patient research, he arrived at results of very indifferent value.

It was not until the time of Galen, a Roman of the second century, that physiology made any noteworthy progress. Following the example of Aristotle, he studied the anatomy of those animals that most closely resemble man in structure, and was thereby led to inquire into the functions discharged by the various organs of the body. Galen had real scientific instinct. He soon perceived that a study of the *dead* is not sufficient to teach us the functions of the *living* body, and he therefore resorted to experiment on living animals. Previous to his time it was supposed that the arteries contain air, because they are found empty after death. It was fancied that the air rushes down the windpipe, and through the arteries, to keep the body cool. Galen exploded this doctrine by simply opening an artery in a living animal, and finding that blood instead of air came forth: a striking illustration of the important physiological knowledge arrived at by *experiment on living animals*. Galen was also the first to state, that the brain, spinal cord, and nerves, must be regarded as the organs of sensation and voluntary motion. He was also the first to point out that the nerves of sensation are distinct from those of motion, and are connected with different parts of the nervous system. He assigned this as the reason why those organs of sense that are capable of voluntary movements, such as the eye and the tongue, have two sets of nerves. "If," says he, "one of these nerves be at any time injured, the organ loses only that function which the injured nerve performed for it; thus, we often see, in one case, the tongue impeded in its motion; and, in another case, in its power of recognising and distinguishing tastes" (*Op.* 26, i. p. 206): an admirable illustration of the important physiological information attainable by the *study of diseased conditions.* Galen, however, fell into numerous errors; but, in spite of these, so far was he in advance of his contemporaries, and so ignorant were his successors, that for centuries his opinions were accepted by all.

No further advancement was made until the revival of learning in the fifteenth century. For some time after this revival mathematics and chemistry were eagerly studied, and it not unnaturally followed that, while the mathematicians attempted to explain all bodily action by mechanical laws, the chemists were equally anxious to show that these might all be accounted for by the chemical action of one constituent of the body upon another. But amidst the purely physical tendencies of the mathematicians and the chemists, the spiritualistic ideas of the Grecian epoch reappeared,—for Paracelsus ascribed the bodily actions to a spirit, supposed to "sit above the stomach." He named it Archæus, or the Spirit of Life, and imagined that it superintends the preparation of the food, and the operations of a number of minor spirits supposed to dwell in the several organs of the body. Such idle fancies availed nothing, but happily, as time ran on, biological thought returned to the channel in which Galen had left it, and the results of observation and experiment again began to drive metaphysical curiosities from the field. The study of human anatomy, begun in Alexandria, but revived in Italy by Vesalius, again prompted earnest inquiry into the real functions of the several parts of the body.

It now came to be the turn of England to advance the science that Greece and Italy had initiated, and through the genius of Harvey she at the beginning of the seventeenth century contributed the greatest of all physiological discoveries—a knowledge of the circulation of the blood. Harvey had studied anatomy in Italy, under Fabricius, but he perceived as clearly as Galen, that a sufficient knowledge of the actions of the living can never be arrived at by merely studying the structure of the dead body. He therefore had recourse to experiments on living animals, and from these was led to discover the circulation of the blood (*Op.* 27, p. 19), and thus to lay the first substantial foundation of physiology, and through this, of the principles and practice of rational surgery and medicine.

It was, however, in Germany, under the influence of Haller, that physiology towards the close of the seventeenth century first rose to the dignity of a science. Possessed of a strictly logical mind, strongly inclined towards physics and mathematics, Haller insisted on eliminating from physiology all statements that could not be verified by observation and experiment. He added considerably to the store of physiological facts, arranged them in the logical order of science, and thus gave to physiology its present aspect. The demonstration by Sir Charles Bell of the different functions of the two roots of the spinal nerves; the discovery of reflex nervous action by Marshall Hall, and of the chemical nature of respiration by Black; the discovery of animal electricity by Galvani; the promulgation of the cell-doctrine by Schleiden and Schwann; the measurement of the blood-pressure by Stephen Hales and Poiseuille; the invention, by Thomas Young, of the graphic method of recording movement, and its application by Ludwig to physiological investigation; the application to physiology of Joule, Mayer, and Helmholtz's principle of the conservation of energy;—these, together with Harvey's discovery, are the keys that have opened the principal gates to the physiology of the present day.

In physiological studies the facts of anatomy, chemistry, and physics form the foundation of the whole; thus, it would be vain to discuss the functions of the parts of the eye, without a knowledge of their structure and mutual relations, and without knowing the laws of optics; for the effect of the crystalline lens upon light is purely physical. Again, it is impossible to comprehend the changes which the food undergoes in its passage through the body without a knowledge of chemistry; for the action of the gastric juice upon the food is a purely chemical problem. But there are phenomena within the body that are restricted to living things, which have laws of their own, and are not explained in the present state of our knowledge by the laws of chemistry or physics—*e.g.*, development, nutrition, sensation, volition, etc. These are termed *vital*, because they are peculiar to living beings. Yet the history of physiology clearly shows that real progress has been made only when the accepted theories regarding *vital* phenomena have been in perfect *harmony* with physico-chemical laws.

Much knowledge of the bodily functions has been attained (1) by merely *observing* vital phenomena in their normal condition. (2) Much more, however, has been learned by *experiments* on animals and on man; for the method of experimentation is far more powerful than that of mere observation in revealing function. Although there are points of specific difference between man and other vertebrates, there are so many points of strict resemblance, that inferences from the results of many physiological experiments performed on dogs, rabbits, frogs, and other animals, are applicable to the case of man. The principal physiological difference between man and the vertebrates immediately below him is to be found in the more highly specialised character of brain action, yet even the physiology of the human brain has been greatly advanced by experiments on the brains of animals. There are other minor points of difference, but it cannot be doubted that the physiology of bone, cartilage, muscle, nerve, and other tissues in a dog or rabbit is essentially the same as in man. Moreover, the heart, blood and lymph vessels, the lungs and kidneys, the liver, salivary glands, stomach, and intestines of a dog or a rabbit discharge functions *essentially* similar to those observed in man. But it must be admitted that there are various differences in points of detail here and there observable; so that although experiments on animals have been of infinite value in human physiology since the time when Galen proved that the arteries during life contain blood, and Harvey demonstrated the circulation of that fluid, nevertheless, in no case can the result of an experiment on an animal be regarded as more than an index of what may *be expected* to hold true in man. It is merely presumptive evidence until its truth is directly proved in his case. Yet so highly is this presumptive evidence valued, that no one would dare to test the effect of some new remedy upon a human being without first of all experimenting with it on animals; for although the effects in the two cases often differ in degree, they are most commonly similar in kind. (3) Physiological knowledge is also arrived at by studying the phenomena of *disease*. Disease may be generally defined as an abnormal physiological condition; in other words, pathology is a modified physiology. Disease works experiments often so refined that they cannot be imitated by art. Thus, from the observation that in some cases of enlargement of the spleen the blood contains an increased number of white corpuscles, the novel conclusion was arrived at that a function of the spleen is to produce white blood-corpuscles. Many other facts in physiology, especially in that of the nervous system, have been derived from this important field of inquiry.

CHAPTER II.

THE MOTION, FORCE, ENERGY, AND WORK OF THE ORGANISM.

THE BODILY MECHANISM.

WITHIN the bodily system there is incessant change. Various kinds of work have to be done. The doing of work implies the expenditure of energy, for energy is the power by which work is accomplished. The expenditure of energy necessitates the renewal thereof, otherwise the working of the body cannot be maintained. In *this* respect the body resembles a machine, such as, *e.g.*, a steam-engine. Every movement of the engine implies the expenditure of power, for the supply of which the consumption of fuel is necessary. In the fuel there is a store of latent power. By chemical change in the form of oxidation the latent power becomes active, heat is evolved, and the machinery driven thereby. In time the fuel is wasted; the volatile products of its oxidation have flown into the air, leaving behind nothing but an ash bereft of all its store of oxidisable material, and therefore robbed of its capacity for work. To maintain the working of the engine it must from time to time be "*fed*" with combustible material and water, "*respiration*" must be allowed in order that the stream of air may supply the requisite oxygen and remove carbonic acid. If sufficiently supplied with fuel, air, and water, the engine would continue to work for an indefinite period but for the circumstance that the machine wears away. The effects of its tear and wear may indeed be remedied by timely repair, but sooner or later it becomes useless and has to be abandoned.

Crude though the analogy be that such a machine bears to the bodily mechanism, the essential lines in both are nevertheless strictly parallel. Every kind of bodily work, from the movement of a limb to the evolution of an idea, implies the expenditure of power, for the renewal of which repeated supplies of food and air are essential. But the bodily system is so curiously and incomprehensibly designed, that, if properly nourished, it *grows* from a comparatively simple speck of jelly-like matter into an apparatus so complex that we cannot with anything like completeness unravel it. The tear and wear of its complicated machinery is in most of its parts for a time fully compensated by self-repair, but sooner or later repair grows tardy and imperfect, the apparatus wears out, and can work no longer.

The incessant ebb of power within the bodily system, implying as it does the consumption of energising material and the tear and wear of tissue, renders necessary the process of nutrition—a process comparatively simple in the lower but excessively complex in the higher animals. It comprehends (1) the means by which new matter is conveyed to the tissues; (2) the transformations it undergoes therein; (3) the manner in which it is removed and thrown away when it becomes useless and effete. The objects of nutrition are to supply material (1) for the building up and for the repair of the bodily system; (2) for yielding energy wherewith to do the bodily work. In analysing the bodily functions we have therefore to keep in view (1) a series of considerations relating to the nature, source, and destiny of the materials employed; (2) another series of considerations relating to the nature, source, and destiny of the energy employed, together with the work it performs.

BODILY MOTION.

The various movements that occur within the bodily system are all, as indeed they must be, merely changes in the relative positions of the masses, molecules, and atoms of its matter, and they result either from the various forces of which the portions of matter are the centres, or from external forces.

1. Ordinary or Visible Motion is produced by contractile tissues, of which muscle is the chief. The functions of muscle and nerve may be conveniently studied in the frog, for as this animal is cold-blooded its muscles and nerves retain vitality for a sufficiently long period after isolation to permit of the performance of experiments. The frog is stunned and pithed to render pain impossible. The skin is then removed, the sciatic nerve is isolated and divided near the spine, and the muscles are removed from the femur, which is then divided. The isolated leg is laid on a plate, or it may be suitably supported by a clamp, as indicated in Fig. 1. This arrangement is well adapted for demonstrating many experiments on muscle and nerve. When the movements of the limb require to be exaggerated, a light lever, such as a straw, may be pinned to the toes.

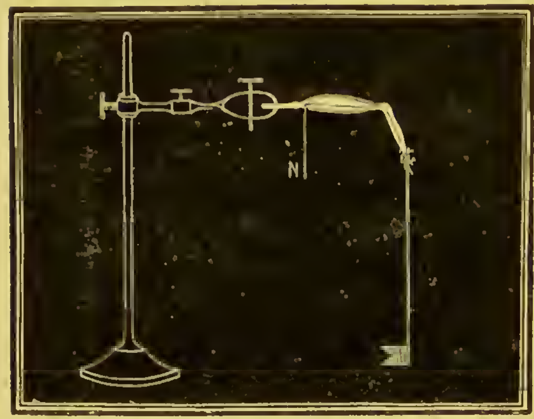


Fig. 1. Frog's limb arranged for experiments on muscle and nerve. N, sciatic nerve.

On applying the electrodes of a Faradic electromotor to the muscle of a living limb so prepared, it is excited by the electricity, and suddenly undergoes a change of shape, becoming shorter and thicker; in a word, it contracts. There is in the substance of each muscular fibre an invisible molecular machinery for the production of mechanical movement.

2. Chemical Motion is a convenient name for the shifting of position whereby atoms and molecules give rise to new combinations. It occurs more or less in every tissue of the body, but principally in the muscular, glandular, and nervous. It must not be assumed that on stimulating the muscle electrical motion is the immediate cause of the contraction, for undoubtedly the electricity acts chiefly if not entirely by setting up chemical change. Chemical motion is as much concerned in causing a

muscle to contract as in driving the bullet from a gun. In the one the electrical stimulus merely induces chemical change, just as the spark, a *thermal stimulus*, merely initiates it in the other. No doubt the case of the gun is far simpler than that of the muscle, for we know by a common experience that with the discharge of the gun the solid explosive substance vanishes, and that, if the introduction of the explosive material be omitted, the spark entirely fails to move the bullet. The muscle is more subtle; its energising material lies hidden within the contractile substance, and so curiously is the apparatus arranged that, unlike the gun, the stimulus does not at once transform *all* the energising material, but discharges with their resultant contractions can be again and again induced, even when the muscle is cut out of the body, and a renewal of the material thus rendered impossible. In time, however, the contractions become feeble, and eventually the stimulus altogether fails to induce them: and this result appears the sooner the greater the intensity and the rapidity of the contractions, for thereby the store of energising material is rapidly used up. We know definitely that chemical change takes place more rapidly in muscle during contraction than during rest, because carbonic acid is rapidly evolved; sarcolactic acid is produced, and changes the reaction of the muscle from alkaline to acid; and there are other chemical changes to be afterwards detailed. We further know that when muscle inside the body is exhausted by repeated stimulation its power may be regained by rest and nourishment, whereby fresh energising material may be introduced, and the effete matter removed.

3. NERVE MOTION.—If the nerve (N, Fig. 1) be stimulated by electricity, or by a pinch, muscular contraction ensues, but there is no visible movement of the nerve; and yet motion of some sort there must be, for the effect of the stimulus travels along the nerve to the muscle. Whether the motion of the nerve particles be a mechanical vibration, or a chemical motion, is unknown, and on that account it is convenient to term it *nerve motion.*

4. SONOROUS MOTION is produced by the vibration of the particles of a contracting muscle; it may be readily heard if the jaws be clenched during the night, when other sounds are hushed. It also arises from the vibration of membranes in the larynx and heart, and to a slight extent in other parts from various causes.

5. ELECTRICAL MOTION is generated by special organs in some fishes, and is also produced in muscle and nerve, and some other tissues, in animals generally. Its source is doubtless chemical motion. In a future chapter the mode of demonstrating the electrical currents of muscle and nerve will be explained.

6. THERMAL MOTION rapidly appears in a muscle when it contracts, in a gland when it secretes, in a nerve cell when it evolves nerve energy, and, indeed, it is produced in all the parts of the body that are the seats of chemical change. In part it springs directly from chemical motion, but it is also immediately derived from the other modes of motion in the organism which all finally assume the form of heat.

7. In addition to the preceding, there are various mechanical movements of a molecular nature; such as the diffusion of liquids and gases, etc.

TRANSFORMATION OF MOTION.

That one mode of motion can give rise to another may be gathered from the preceding, and it may be further illustrated as follows:—1. On rubbing a resinous rod with a piece of flannel, the mechanical movement of the dissimilar substances gives rise to electrical motion; the two electricities in the resin are separated, the negative remaining in that substance, while the positive electricity passes into the flannel. If the electrified resin be brought near a pith ball suspended by a thread, the negative electricity of the former attracts the positive electricity of the latter, and thereby causes a mechanical movement of the ball towards the rod. 2. On beating, *e.g.*, a piece of lead with a hammer, the mechanical gives rise to thermal and sonorous motions. 3. On striking together flint and steel, the mechanical motion produces heat and light. 4. That heat can produce mechanical motion is readily shown by the bubbling of boiling water. 5. That heat can occasion electrical motion may be proved by heating a thermopile. This consists of bars of dissimilar metals, such as bismuth and antimony, two ends of which are soldered together like the letter V, while the free ends are joined to the wire of a galvanometer. On heating the junctions of the metals, the two electricities are separated, and the current reveals its presence by deflecting the needle of the galvanometer. 6. That electrical motion can generate heat and light may be shown by conducting the current from a large Bunsen's cell along a thin platinum wire. The powerful resistance that the wire offers to the electrical motion leads to the production of intense heat and light. 7. The burning of any combustible material shows that chemical motion can give rise to heat and light. These elementary facts in physics are recapitulated here merely to render clear what follows.

FORCE.

The nature of force is unknown. Looking to its effects, it is defined as that which produces, accelerates or retards, or changes the direction of motion. As force is an attribute of matter, and since the matter of living things can only be derived from the non-living world, it follows that the various forces—*e.g.* gravity, cohesive, adhesive, and repulsive forces, chemical affinity, electrical force, and others displayed by matter in the non-living—are also found in the living world. Although the motions of things living lead to results in many instances widely different from those met with in inorganic nature, yet there is no evidence whatever that these are due to agents other than the ordinary forces of matter.

All forces being either attractive or repulsive, diminish or increase the distance between portions of matter. That force produces motion needs no illustration. That it can prevent motion is readily proved by attempting to overcome the force of gravity in lifting a heavy weight. Further, in attempting to distort a solid body, the cohesive force of its particles offers more or less resistance to the external pressure. In such cases the force of the opposing body is for convenience termed a *force of* *resistance.* That force may *retard* motion is illustrated by any case of friction.

We have seen that one mode of motion can be transformed into another. That is to say, the various modes of motion are correlated. There is, however, no reason for believing that the transformation of force is possible; there is no evidence that gravity or cohesive force can give rise to chemical force; nor this to any other form of force. As far as we at present know, the several forces are distinct attributes stamped on matter by its Creator. The terms "transformation of force" and "correlation of force" are therefore no longer admissible. They were adopted when the term force was used to signify the energy of motion as well as that which occasions motion.

ENERGY AND WORK.

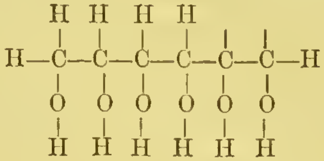
WORK.—Energy is the power of doing work. Work is the act of producing motion against resistance (Maxwell). Thus work is done when a weight is lifted; because gravity resists the change. Work is done when a solid is melted into a liquid, because cohesive force resists the change; or when a gas is compressed work is done in overcoming the repulsion of its molecules. In contractile tissues the work is principally mechanical. In glands it is chiefly chemical. In the brain the nature of the work is not comprehended. We can readily conceive how chemical change in a nerve cell can set up nerve-motion, and do work which may end in exciting a muscle to contract, or a gland to secrete, but we are entirely ignorant of the nature of intellectual work. In some way or other it depends on material movement, because the molecules of such a substance as chloroform can suspend its production, and they can only do this by acting on the material substratum concerned in the production of sensations and ideas. Doubtless they inhibit or suspend the production of these states of consciousness, by suspending the chemical or other motions necessary for their production. The evolution of an idea is as certainly a work of the nervous apparatus, as a mechanical movement is the work of a muscle; but while we can readily perceive that mechanical work is a shifting of material position against some resisting force, we have not the least comprehension of the manner in which the motions set up in the brain give rise to consciousness and other psychical phenomena. The real nature of mental work is therefore an unsolved problem.

ENERGY is neither force nor motion, but it implies the existence of force and its power of producing motion. For example, when a weight rests on the earth it has no energy, although it is influenced by the force of gravity. When lifted, and held at rest in the air, it has no motion, and the force of gravity is scarcely so powerful as when the weight lay on the earth. Nevertheless, it now possesses *potential* energy; that is, energy *in virtue of its position* with reference to the earth. If now the weight be allowed to fall, its energy becomes *actual* or *kinetic;* that is, energy *in virtue of motion.* Seeing that kinetic (κινέω, to move) energy implies motion, the various modes of motion are for convenience spoken of as forms of kinetic energy. Take now such a case as that of carbon and oxygen. When their atoms are locked together in the form of carbonic acid, they, like the weight resting on the earth, have no energy. But if by some power the atoms be torn asunder, they, like the weight lifted and held apart from the earth, acquire potential energy—in virtue of their position of relative distance. When a suitable temperature permits of their reunion, they rush together, and in so doing, their potential energy vanishes, while the kinetic energy of chemical motion appears. In gunpowder there is a magazine of potential energy in virtue of a certain relative position of its constituent molecules, in consequence of which, they—when their movement is initiated by a spark—rush into new combinations. Potential energy then disappears and gives place to the actual or kinetic energy of chemical motion, and this in turn produces the kinetic energies of heat and mechanical movement.

TRANSFORMATION OF ENERGY.—As kinetic energy is the energy of motion, and the various modes of motion are termed kinetic energies; therefore, one form of kinetic energy can be transformed into another. Moreover, potential can give rise to kinetic, and this in turn to potential energy. Thus in lifting a weight, kinetic energy vanishes, and its equivalent of potential energy appears. When the weight falls, its potential energy disappears, and its equivalent of kinetic energy is obtained.

In the potential state there is no motion; because the tendency to move is overcome by some force of resistance. Thus in the case of a weight held at a distance from the earth, the force that resists the passage of the potential into the kinetic state is in the support. The resistance that prevents the atoms of carbon and oxygen from uniting at the ordinary temperature is probably to be found in the attraction by which the atoms of carbon cling together and form molecules, and similarly in the case of oxygen. A power that can overcome the resisting force is needed to liberate a body from the potential, and allow of its passing into the kinetic condition. Such a power is termed a *liberating energy.* Thus, the withdrawal of the support liberates the suspended weight; the pulling of the trigger liberates the bent crossbow; a spark liberates the energy of the gunpowder; an electrical or nervous stimulus, when applied to muscle, liberates the potential energy of its chemical material. In all these cases the liberator is some form of kinetic energy, whose work may be merely that of overcoming the resisting force; just as the liberator who opens the door of a prisoner's cell merely overcomes the resistance it offers to his escape, and does not supply the energy with which he goes hence.

RELATION OF PLANT TO ANIMAL.—As regards energy, plant and animal are related thus:—The sun's light and heat enable the tissues of the green plant to break up carbonic acid and to build up the carbon with other elements derived from water, ammonia, etc., into complex organic molecules, some nitrogenous, others non-nitrogenous. These are stores of potential energy, because the atoms of carbon, hydrogen, nitrogen, and, it may be other elements, are in such mutual relation that their chemical affinity is only partially satisfied. Thus, take such a comparatively simple case as that of grape-sugar. The hypothetical relations of atoms in the molecule, $C_6 H_{12} O_6$ may be thus represented :—

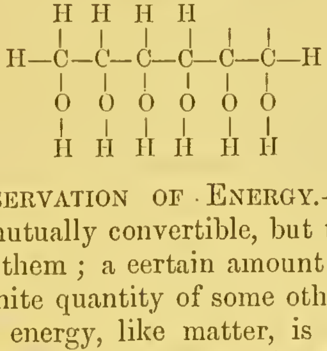


$$\begin{array}{ccccccccccccccc} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & & & & & \\ & & | & & | & & | & & | & & | & & | & & \\ \mathrm{H} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{H} \\ & & | & & | & & | & & | & & | & & | & & \\ & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \\ & & | & & | & & | & & | & & | & & | & & \\ & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

The graphic formula indicates that in the molecule the position of the carbon atoms is such, that they are probably linked one to another and to hydrogen. But the attraction of carbon and hydrogen for oxygen is far more powerful than either that between carbon and carbon, or between carbon and hydrogen ; therefore, when the sugar is burned, every atom of carbon and of hydrogen becomes fully linked with oxygen, carbonic acid and water being the *material*, and the evolution of heat the *kinetic* result. Such a change doubtless takes place when the sugar is burned in the animal organism, and therefore it may be stated generally, that while *the plant accumulates potential, the animal transforms this potential into the various kinetic energies* of the body, all of them finally becoming heat and radiating into space.

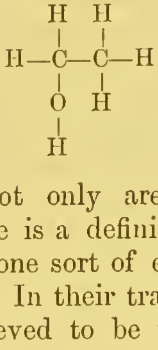
The principal chemical change in the animal body whereby the potential energy of the food becomes kinetic is undoubtedly oxidation ; but this is not the only source. It is also produced whenever a complex organic molecule merely splits up into simpler molecules in which the atoms are so rearranged that their mutual affinities are more perfectly satisfied. Such a change is illustrated in the alcoholic fermentation of grape-sugar. It is commonly stated that a molecule of grape-sugar ($C_6 H_{12} O_6$) splits up into two molecules of alcohol ($C_2 H_6 O$) and two of carbonic acid (CO_2) ; but Pasteur has shown that small quantities of glycerine, and succinic acid are also produced ; nevertheless, as alcohol and carbonic acid are the chief results, only their composition need be contrasted with that of the sugar, in considering the changes. From the following graphic formulæ it appears that the affinities of the carbon, at all events, are more satisfied by the change, the energetic result of which is the evolution of heat.

Glucose.



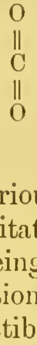
$$\begin{array}{ccccccccccccccc} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & & & & & \\ & & | & & | & & | & & | & & | & & | & & \\ \mathrm{H} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{H} \\ & & | & & | & & | & & | & & | & & | & & \\ & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \mathrm{O} & & \\ & & | & & | & & | & & | & & | & & | & & \\ & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & & \end{array}$$

Alcohol.



$$\begin{array}{ccccccc} & & \mathrm{H} & & \mathrm{H} & & \\ & & | & & | & & \\ \mathrm{H} & — & \mathrm{C} & — & \mathrm{C} & — & \mathrm{H} \\ & & | & & | & & \\ & & \mathrm{O} & & \mathrm{H} & & \\ & & | & & & & \\ & & \mathrm{H} & & & & \end{array}$$

Carbonic Acid.



$$\begin{array}{c} \mathrm{O} \\ \| \\ \mathrm{C} \\ \| \\ \mathrm{O} \end{array}$$

CONSERVATION OF ENERGY.—Not only are the various forms of energy mutually convertible, but there is a definite quantitative relation between them ; a certain amount of one sort of energy being equivalent to a definite quantity of some other. In their transformations nothing is lost, for energy, like matter, is believed to be indestructible ; or as it may be otherwise expressed, *the sum of the potential and kinetic energies of the universe is constant.* This is the law of the conservation of energy. This law, though elaborated by Helmholtz and others, was founded on experiments made by Joule, who proved the quantitative equivalence of heat and mechanical movement. He found that when a pound of water falls through a height of 772 feet, its temperature is raised 1° Fahr., and that if the amount of heat necessary to elevate the temperature of one pound of water 1° Fahr. be converted into ordinary motion, it can lift one pound to the height of 772 feet from the surface of the earth.

The principle of the conservation of energy has been proved to be a law in the inorganic world, but owing to the excessive difficulty of the problem, especially as regards the estimation of nerve-energy, its universal truth in physiology has neither been proved nor disproved. But as every definitely ascertained fact is in harmony with the principle, it is *provisionally accepted as a probable hypothesis on which to proceed;* and when we consider that a denial of the law implies that the *living alone amongst things material have the power of creating or destroying energy, and seeing that they certainly have not this power over matter*, we cannot but prefer to entertain the hypothesis that the law of the conservation of energy extends to vital operations.

DISSIPATION OF ENERGY.—When the bow is drawn across a violin string the mechanical energy is not entirely converted into sound, but a portion of it is through friction *dissipated* into heat—a useless form of energy in this particular instance. Again, in winding up a watch, the spring does not obtain the full equivalent of the mechanical energy employed, because through friction a portion is dissipated into heat. All energy tends ultimately to assume the form of heat, and as such dissipates away from every working system. Thus in the body the chemical energy of the food produces mechanical, nervous, and other energies; ultimately, however, all are transformed into heat that dissipates away into space.

MEASUREMENT OF ENERGY.—Energy being the power of doing work, its quantity may be indicated by the amount of work. Quantities of mechanical energy are indicated by units of mechanical work. The English mechanical unit is the *foot-pound;* that is, the amount of energy required to raise one pound to the height of one foot from the earth's surface. The metric mechanical units are the *kilogrammeter*, the *gramcentimeter*, and the *grammillimeter*, these indicating respectively the amounts of energy needed to lift a kilogramme to the height of a meter, and a gramme to the height of a centimeter or a millimeter.

Quantities of thermal energy are expressed in heat units. The English heat unit is the *pound-degree;* that is, the amount of heat required to raise one pound of water 1° Fahr. The metric units are the *kilogram-degree* and the *gram-degree;* these respectively indicating the amount of heat needed to raise a kilogramme and a gramme of water 1° C. From Joule's discovery—already alluded to—of the definite quantitative relation between mechanical and thermal energy, 772 foot-pounds are equivalent to 1 pound-degree; that is, the heat required to raise one pound of water 1° Fahr. could, if entirely converted into mechanical work, lift one pound to the height of 772 feet. On the metric system the mechanical equivalent of 1 *kilogram-degree* is 424 *kilogrammeters.*

The three great working systems of the body are the *muscular*, the *glandular*, and the *nervous*. 1. Muscular work being mechanical is readily expressed in mechanical units. Thus, if we hook a weight of say 20 grammes to a frog's muscle, excite contraction, and observe that the weight is lifted say 2 millimeters, then $20 \times 2 = 40$ grammillimeters of work. 2. The work of a gland is to produce a secretion. Many of the substances found in secretions are produced within the gland tissue, while others are merely abstracted by it from the blood. But whether producing or merely abstracting, the work of the gland is indicated by the amount of each constituent that enters the secretion in a unit of time. 3. In the nervous system the estimation of its work has as yet been only roughly indicated. Seeing that all energy ultimately assumes the form of heat, one might anticipate, on theoretical grounds, that the energy of nerve motion as it sweeps through a nerve would be indicated by the extent to which the nerve becomes heated. But the heat evolved is so small in amount that some reliable investigators have failed to detect it. The intensity of the excitement of a nerve is therefore approximately indicated by observing the effect it produces on a terminal organ, such as a muscle, or by measuring the amount of electrical disturbance set up in a nerve during its excitement by the method to be afterwards described.

But in *intellectual processes* we have no means of measuring the energy expended. We are as certain that it requires more work to sum up a hundred than to sum up ten figures, as we are of the fact, that more mechanical work is needed to lift a weight one hundred than to lift it ten feet. But while we know that to lift the weight one hundred feet is just ten times the work of lifting it ten feet, we cannot say the same of the addition of the figures, for the summation of 2, 2, 2, 2, requires from most persons less work than the summation of 9, 7, 8, 7. Unlike mechanical work, mental work is extremely varied, and it is only roughly estimated by standards of the most arbitrary kind. The rough ideas regarding mental work arrived at by common experience are, however, of great value in the ordinary routine of life and in practical medicine. Thus, if we have to deal with a person whose brain-power has been weakened by disease, we are careful to reduce his brain-work to a minimum. We take care that if he reads at all it shall only be light literature. In conversation we avoid all topics that would compel him to think deeply. We refrain from asking questions that would tax his memory. All argument is carefully avoided. We would never expect such a person to work out a complicated mathematical problem or to make a speech, because it is an everyday experience that these require vigorous mental effort. But although we have some idea of the quantity of work that this or that mental exercise requires, it is at best so rough and indefinite that the exact measurement of mental work is really quite outside the domain of exact science.

Physiology is not an exact science like physics and chemistry, because we cannot accurately measure all the various kinds of work that an individual can perform. We cannot predict that two individuals apparently similar, who consume the same daily amount of the same food, will be able to perform the same amount of work, even when, as in the case of mechanical work, it can be measured with tolerable accuracy. We cannot even predict that the same individual will be able to perform the same amount of the same kind of work from day to day, even when he consumes food similar in quantity and quality. We cannot even predict that if the same stimulus be applied to two nerves, the amount of excitement will be the same in both. From some cause unknown to us the one nerve may be more irritable than the other, and on that account suffer greater excitement. The organisation of animals, even of the same species, is in its finer details infinitely varied. Some of their machinery, especially the nervous and glandular, is readily affected by various conditions that modify the working power in a manner and to an extent so obscure that it would be impossible to accurately predict the work that can be done, even if that work could be exactly gauged. Certainly physiology will yet become much more exact than it is at present, but it may safely be predicted that complete exactness in every department will never be attained.

CHAPTER III.

THE USE OF THE MICROSCOPE.

The magnifying powers of the microscope commonly employed in histological (ἱστός, web) studies vary from about 50 to 1500 diameters linear. Still higher powers are sometimes had recourse to, but the properties of light itself, apart from the difficulty in constructing lenses of very high power, render them of no very great service; indeed, the investigations of Abbe (*Op.* 9, xiv. p. 191) and of Helmholtz (*Op.* 9, xvi. p. 15) show that the lenses now constructed have, as regards magnifying powers, reached the limit of usefulness; and that there is little to be gained by employing lenses that magnify more than 1500 diam.; for, above this power, the delusive effects of diffraction became very serious—so much so, that no microscope has yet been constructed, nor will it ever be (Abbe), with a useful magnifying power that reaches 4000 diam. If such be the case, it is calculated that objects less than $\frac{1}{180000}$ inch must remain invisible; and although Dallinger's (*Op.* 9, xvii. p. 224) observations show that this limit determined by mathematical calculation is rather too narrow, there seems no reason for supposing that it is likely to be very materially extended. We must, therefore, rest satisfied with the thought that we can only see *masses* of matter that are immensely larger than the *molecules* of which they are composed. The *finest structure of molecular mechanisms must remain invisible.* One must, therefore, guard against the supposition that identical physiological properties must belong to things that have an apparently similar structure when seen with an instrument so limited in power as the microscope—*e.g.*, it reveals no noteworthy difference between the germ of a rabbit and that of a dog; and yet, from observing the results of their activity, we are obliged to conclude that there must be some essential difference between them. This instrument, then, deals with tolerably large masses of matter; revealing their configuration when their outlines are evident, and their *visible* movements when these are of sufficient extent.

THE SIZE OF MICROSCOPIC OBJECTS is in this country commonly indicated in fractions of an inch. On the Continent the unit of microscopic size now commonly adopted is the *micro-millimeter.* This unit is the one thousandth of a millimeter (0·0000397 inch). In writing it is indicated by the letter μ, and in speaking may be conveniently shortened to *micro.* The human blood-corpuscle being a well-known object, and of tolerably constant size, its breadth is sometimes for convenience used as the histological unit. Its broad diameter is $\frac{1}{3200}$ inch, or 8 μ.

GRANULE, GLOBULE.—A granule is a particle of indefinite shape and size, but so minute that it must be magnified 200 or 300 diam. to render it visible. If such a particle be uniformly dark without any light centre, it may be termed a *fine granule* (*a*, Fig. 2), while if it have a light centre with a dark outline (*b*), it may be termed a *coarse granule.* That this variation in optical character is simply the result of a difference in size is proved by the fact that when *a* is more highly magnified, it presents the characters of *b*, and conversely, when *b* is less highly magnified, it presents the characters of *a*. The term *globule* is applied to a particle having, like the coarse granule, a clear centre with a dark margin, but possessing a globular shape (*c*).

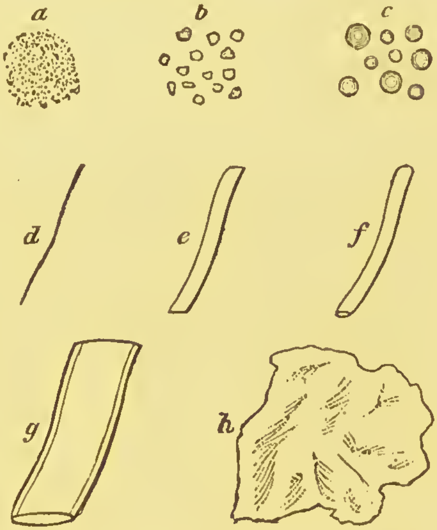


Fig. 2. *a*, Fine granules; *b*, coarse granules; *c*, globules; *d*, fine fibre or fibril; *e*, coarse fibre; *f*, fine tubule; *g*, coarse tubule; *h*, membrane. *Magnified 300 diam.*

FIBRE, FIBRIL.—A fibre is an elongated thread-like body. If it be extremely fine, it presents nothing but a dark line without any light centre (*d*, Fig. 2). To a fibre of such tenuity the term *fibril* is often applied. If the fibre be of relatively greater breadth, it has a light centre bounded on each side by a single dark outline (*e*).

TUBULE, MEMBRANE.—A tubule presents a light centre bounded on each side by a single dark outline, if the wall be exceedingly thin, or if a low magnifying power be employed (*f*, Fig. 2); but if the wall be of considerable thickness, or if the magnifying power be high, a double contour may be seen on each side of the clear centre (*g*). But if it happen that the contents of the tubule have a refractive index the same or nearly the same as that of the wall, it may be impossible to see a double contour even when the envelope is tolerably thick, because of its inner margin being undefined. The term *membrane* is applied to any sheet of tissue (*h*). It may present a homogeneous, fibrillated, or other appearance. It may form the wall of a tube or cell, or be otherwise extended. When excessively thin, its edge shows only a single dark line, but if sufficiently thick, or if it be very highly magnified, it shows a dark outline with a clear band in the centre. It may be gathered from the preceding, that microscopic appearances very largely depend on two variables—the *magnitude of the object* and the *magnifying power employed*, and that the necessarily vague terms *fine* and *coarse* are merely adopted for convenience of description. Generally speaking, however, the bodies *a*, *d*, and *f* (Fig. 2) are described as *fine*, because of the characters they exhibit under the ordinary medium magnifying power of 300 diameters.

CHAPTER IV.

THE CELL.

PROTOPLASM.

THE lowest living forms, of which the protamœba (Fig. 3) is an example, consist of simple undifferentiated protoplasm, and nothing more. Protoplasm is also found in the tissues of all plants and animals, however complex. It may be advantageously studied microscopically in certain cells of the tradescantia plant (Fig. 5), in the white blood-corpuscles of the newt (Fig. 13), as well as in the amœba and protamœba. Protoplasm, considered *physically*, is a colourless, transparent jelly-like substance, that may be finely granular or hyaline. Its consistence varies, being in some cases semi-fluid, and though in others it preserves a definite form, it is always soft. Although apparently structureless, it must be maintained as a *hypothesis* that the molecules of the various substances of which it consists are not thrown together indefinitely, but form an organised molecular machinery, capable of invisible and visible movements, that give rise to the phenomena of life. Protoplasm is rendered excessively hyaline, and may disappear, in acetic acid or in caustic alkali. It usually has a marked affinity for such pigments as carmine, logwood, and rosaniline nitrate (magenta). Considered *chemically* it has a very complex but not definitely ascertained composition. As *living* protoplasm cannot be subjected to chemical analysis, its composition is merely inferred from that of protoplasm analysed as soon after death as possible. Knowledge thus attained, however, can only be approximative, for *instability* is a prominent characteristic of complex *nitrogenous* organic compounds, and at death they in some instances certainly undergo change. Protoplasm contains albuminous or proteid substances as its chief solid constituents. There are

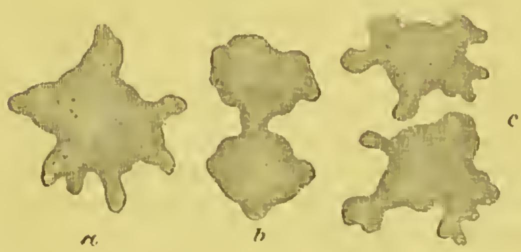


Fig. 3. *Protamœba.* *a*, In its ordinary state; *b*, dividing; c, divided. × *about* 1000 *diam.* (Hæckel.)

always small quantities of carbohydrates, of fat or its allies, of mineral salts, and a large quantity of water. Like albumin, protoplasm is coagulated by heat. Living protoplasm is the arena of complex chemical changes which are very imperfectly known. Considered *physiologically*, protoplasm is the physical substratum of life. It is excitable or irritable, and when its molecular machinery is excited it becomes the seat of motions that lead to results characteristic of vitality. In *all* cases there are the invisible molecular movements that lead to *nutrition* and *growth ;* also, there is, at some period or other of the existence of the protoplasm, a visible movement that ends in the *multiplication* or *reproduction* of the protoplasmic mass. Thus, when the protamœba multiplies, its protoplasm becomes as it were constricted, and finally separates into two masses, each one a protamœba (Fig. 3). In many cases the protoplasm exhibits visible movements not ending in multiplication, but merely in a locomotion of the whole or a part of the protoplasmic mass. Thus in some vegetable cells (Fig. 6) a streaming movement of the protoplasm is observed. In free masses of protoplasm, such as protamœba, amœba, and white blood-corpuscles, the protoplasm streams indefinitely in this or that direction, causing indefinite changes of shape in the mass. This kind of protoplasmic movement, being so typically illustrated in the amœba, is termed amœboid. In complex living things, movements that lead to differentiation or evolution occur in protoplasm, whereby there arise protoplasmic masses that differ widely in function ; some evolving nerve-energy, others producing mechanical energy, others secreting bile, urine, and so on. These different acquirements seem to result from some subtle change in the molecular constitution of the protoplasm. Various other differentiations of protoplasm may take place, but these can only be studied in the sequel.

The various agents by which living protoplasm can be excited and thrown into motion are termed in this connection excitants, stimulants, or irritants. They are always forms of kinetic energy, *e.g.* thermal, electrical, mechanical, and chemical. Their special effects, however, will be afterwards studied.

YEAST.

Many facts having a general bearing may be gathered from a study of some simple plant, such as the yeast of beer (*Torula Cerevisiæ*) in a state of active growth. The average size of the fully-developed torula being only $12\ \mu$ ($\frac{1}{2000}$ inch), it is necessary to magnify it at least 300 diameters to discern its structure, and it is very advantageous to use a magnifying power of 1000 or 1200 diam.

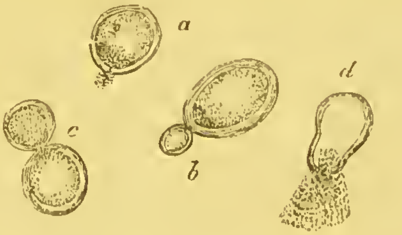


Fig. 4. *Torula Cerevisiæ.* Torulæ with (*a*) young, (*b*) older, (*c*) still older bud ; *d*, torula ruptured by pressure. × 1200.

Structure of Yeast.—Each torula is a rounded or oval corpuscle, consisting of a thin envelope enclosing a finely-granular, colourless substance, having a slightly dim appearance like ground glass (*a*, Fig. 4). The envelope, notwithstanding its tenuity, is remarkably tough, but by forcible pressure between two slips of glass it may be ruptured and its contents expelled (*d*). The contained matter is protoplasm. In the larger torulæ there are usually one or more vacuoles. These are merely spaces containing fluid that appear in the protoplasm as the torula grows. Vacuoles are far more common in the protoplasmic masses of plants than in those of animals.

The protoplasm has a remarkable affinity for some pigments. Rosaniline nitrate (magenta) and carmine redden it, logwood renders it violet. On the other hand, the envelope seems to have no affinity for these dyes. It should be stated, however, that when a concentrated solution of the staining agent is employed the envelope necessarily acquires a tint, apparently not because of any attraction for the dye, but merely from its being permeated by an intensely coloured fluid. The dye brings into view a nucleus amidst the protoplasm of some of the larger torulæ, but its presence is by no means constant.

A solution of osmic acid blackens particles of fat that are usually present in the protoplasm.

Acetic acid and solutions of caustic alkali have no effect on the envelope of the torula, but they render the protoplasm so clear that, after a time, it becomes impossible to see anything but a few granules in its place. This is due to the envelope being chiefly composed of cellulose, while the protoplasm principally consists of proteid matter.

DEVELOPMENT OF YEAST.—There is no proof that a torula ever originates spontaneously. It certainly, however, springs from a parent in the form of a bud. A very careful examination of a germinating torula, magnified about 1000 diam., is required to trace the manner in which the bud grows, and the use of a staining agent is indispensable. The bud, in its youngest state, is a particle of protoplasm continuous with that of its parent, through a minute aperture in the envelope of the latter (*a*, Fig. 4). The protoplasm of the parent seems to be the only part concerned in germination, the sac being passive. No sac is discernible around the bud in the first instance, but ere long it appears, extremely thin at first, but thickening as the bud enlarges (*b*). It is certain that the sac is not a deposit from the surrounding fluid, for the torula grows in fluids that contain no cellulose. Nor is there the least evidence that the young envelope grows around the bud from the parent sac, but it seems quite certain that it is produced by the protoplasm which it envelopes. It cannot be maintained, in this case at all events, that the outer part of the protoplasm becomes transformed into the envelope, for the latter consists chiefly, if not entirely, of cellulose ($C_6 H_{10} O_5$); while the protoplasm is principally composed of proteid matter, that contains both nitrogen and sulphur, in addition to carbon, hydrogen, and oxygen. How the cellulose is formed by the protoplasm is unknown; all that we can say is, that it in some way or other *secretes* cellulose, or a substance that becomes cellulose, the molecules of which find their way out of the protoplasm and accumulate on its surface.

As the bud grows older it enlarges, owing to an increase in the mass of its protoplasm and of its cellulose sac. In time a vacuole appears; and before or after this the bud in turn germinates. The parent torula, and each of its offspring, may produce three or four buds, which hang together for a considerable time in irregular chains and clusters. After the torula has budded to its full extent, its protoplasm atrophies, and eventually disappears, leaving its passive shell empty. There is, therefore, in the life-history of this comparatively simple individual, a period of active growth, followed by a period of decline, and finally by death. The torula is—1, a particle of simple protoplasm; 2, a particle of protoplasm in a cellulose envelope; 3, an envelope from which the protoplasm has vanished. In the first stage it is undifferentiated in structure; in the second, structural differentiation has taken place; in the third stage the protoplasm, the cause of growth, has vanished.

PROTOPLAST AND PERIPLAST.—It is convenient to apply the term *periplast* to the envelope of a protoplasmic mass, whatever be its chemical nature or its physical aspect. The advantage of employing this term will afterwards appear, when it is seen that in fibrous tissue, the homologue of the torula envelope is a bundle of fibrils; while in the enamel fibres of a tooth, it is a solid prism of matter chiefly calcareous. Adopting this nomenclature, the three structural phases in the life-history of the torula may be thus classified: 1. A simple protoplast. 2. A simple or nucleated protoplast with a periplast. 3. A periplast only.

THE CELL.—The torula is a "unicellular organism;" that is, it consists of a single morphological unit—a cell. The most complex plants and animals are merely aggregations of the morphological unit variously arranged and variously modified. The units differ in structure, but they are all either (1) a protoplast, simple or nucleated, without a periplast; or, (2) a protoplast, simple or nucleated, with a periplast; or, (3) a periplast from which the protoplast has disappeared. In the sequel the different significations that have been attached to the term *cell* will be indicated; but for the present it is enough to say that we shall use it to indicate *the morphological unit*, preferring the term cell to any other, on account of its historical significance, and also because it is short and convenient.

CHEMICAL COMPOSITION OF YEAST.—Like every other living thing, yeast consists of (I.) *organic* and (II.) *mineral* matters. The *organic* substances are — 1. Proteid or albuminous and albuminoid substances. What proteids are present in this particular instance has not been fully ascertained; but at all events they resemble albumin in having highly complex molecules, containing C H N O S in quantities not precisely known. There is also an albuminoid matter named nuclein (Hoppe-Seyler, *Op.* 28, p. 84) that contains C H N O P, but whose formula is not yet settled. 2. A carbohydrate in the form of cellulose ($C_6\ H_{10}\ O_5$). 3. Neutral fat ($C_?\ H_?\ O_?$), the composition of which has not been determined in this particular instance; lecithin, an azotised fat ($C_{44}\ H_{90}\ N\ P\ O_9$); and cholesterin ($C_{26}\ H_{44}\ O$), an alcohol, but allied to the fats (Hoppe-Seyler, *Op.* 28, pp. 79, 81). 4. The mineral matters are water, potassium phosphate, calcium phosphate, and magnesium sulphate.

When the torula is burned, its organic matter is oxidised, and otherwise resolved, the carbon uniting with oxygen to form carbonic acid, the hydrogen with oxygen to form water, and with nitrogen to form ammonia, while the sulphur of the proteids and the phosphorus of the nuclein and lecithin unite with oxygen and hydrogen to form sulphuric and phosphoric acids, which combine with bases and remain in the ash with all the other mineral matters save water. It therefore appears that a part of the sulphur and phosphorus in the ash, formed elements in the *organic* matter of the torula; from which it is evident that there is no sharp line of demarcation between matters termed mineral or inorganic and those termed organic.

Were the torula eaten by an animal and slowly burned within its body, the results would be similar to those of the more rapid oxidation, with the exception of the ammonia, which would be mainly represented by urea ($CH_4 N_2 O$), a substance closely related to ammonia. Within the torula the above substances are so distributed that the envelope is composed of cellulose saturated with water containing salts, while the protoplasm consists of the other organic matters above mentioned, together with salts and water.

NUTRITION AND GROWTH OF YEAST.—*Food.*—The torula grows readily in a fluid containing

Oxygen.
Water ($H_2 O$).
Cane sugar ($C_{12} H_{22} O_{11}$).
Ammonium tartrate ($C_4 H_4 (NH_4)_2 O_6$).
Potassium phosphate ($KH_2 PO_4$).
Calcium phosphate ($Ca_3 P_2 O_8$).
Magnesium sulphate ($Mg SO_4$).

This is a modification of Pasteur's fluid, devised by him[1] for the cultivation of fungi. The torula grows best when sugar is present in the above fluid, but it also grows when the sugar is omitted, with this difference in the result, that when sugar is absent the torulæ contain no neutral fat (Pasteur). As the case is simplified by omitting the sugar, we will simplify the case by ignoring its presence.

Assimilation.—The torula, unlike plants containing chlorophyll, needs no *light*, but the molecular machinery of its protoplasm can do nothing with food-material unless it be excited and kept in molecular movement by a suitable amount of *heat*, 25-35° C. (77-95° F.) Influenced by heat the protoplasm becomes the seat of *metabolism*,[2] decomposes ammonium tartrate and sulphuric acid, and possibly water, and builds up their C, H, N, O, and S, into molecules of proteid matter of unknown but certainly of very complex composition. This action of the protoplasm is the *chemical* phase of its *assimilative* power, and seeing that this is a plant, its metabolism chiefly consists in the *integration* of complex molecules from those that are relatively simple.

Yeast is considered to be a plant because its protoplasm has the power of integrating complex organic molecules, and also because its periplast consists of cellulose. Yet yeast differs from higher plants inasmuch as it can, like an animal, take its nitrogen from pepsin (Mayer), a substance allied to albumin; indeed, it thrives better on this than on any other substance known. Ordinary albumin, however, is ill adapted for its food. As regards the cellulose of the torula, it might be supposed that it is produced from the sugar of Pasteur's fluid, but the fact that the torula grows and multiplies when sugar is omitted suggests that it is in some way or other derived from the proteid material of the protoplasm. Lecithin and cholesterin are also probably derived from the proteid matters. Very probably, however, the neutral fat is, under protoplasmic influence, derived from sugar, for, as already stated, it is not produced when sugar is absent.

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[1] Pasteur used yeast ash in place of the minerals mentioned in the text (*Op.* 13, vol. xlvii. p. 1011).

[2] This term was first used by Schwann (*Op.* 29, p. 193) to signify the chemical changes that take place in organisms.

But the *assimilative power* of a living organism has a *physical* as well as a *chemical* aspect. The substances that have been *chemically assimilated* by the torula are built up into structure. Some are added to the protoplasm, while others pass out of this and are formed into a firm envelope. This molecular aggregation—which constitutes *growth*—results from a *plastic power* in the molecules concerned. In a crystal, growth also results from a plastic power that is obviously due to the *physical* forces of its molecules. The growth of the living particle, however, differs in detail very notably from that of a crystal; for while the latter grows by the mere *accretion* (superposition) of *homogeneous* particles, the torula grows *from within, heterogeneous* molecules being variously located in the process. This mode of growth, so characteristic of vitality, was, like chemical assimilation, formerly ascribed to a hypothetical *vital force.* But just as *chemical assimilation* is now ascribed to the chemical forces of the atoms and molecules concerned, so *plastic assimilation* is ascribed to their physical forces. The death of the torula protoplasm, which takes place after a certain period of life, notwithstanding a supply of suitable food and exposure to otherwise normal conditions, probably results from a failure of assimilative power.

Disassimilation.—Plant metabolism, although very largely integrative, is however not entirely so. The disintegration, or regressive metamorphosis, of complex organic molecules by oxidation—so marked a feature in animal metabolism—is indeed in abeyance, yet evidence of its presence is to be found in the similar character of the respiration of plant and animal protoplasm. Both absorb oxygen and excrete carbonic acid, and although, in the animal at all events, carbonic acid may result from the oxidation of substances that have never been assimilated into tissue, yet there can be no doubt that its formation is largely due to the *disassimilation* or disintegration of molecules that, for a time, played their part in the living tissue.

As respiration occurs in the protoplasm of plants generally, it is inferred that it also takes place in torula, and when it grows, as it certainly can, without the presence of free oxygen, it is conjectured that it obtains oxygen from sugar. It is only when chlorophyll is present in the plant that there is superadded to the above process the decomposition of carbonic acid and the exhalation of oxygen by the chlorophyll when influenced by light.

The two processes of *assimilation* and *disassimilation* take place in every protoplasmic mass—whether of plant or animal. When the two processes are exactly balanced, there is no change of bulk; when assimilation is in excess, growth is the result; while, on the other hand, atrophy or wasting, and death ensue when assimilation grows feeble, and the forces that produce disassimilation obtain the mastery.

The remarkable power that yeast possesses of transforming cane into grape sugar, and the latter into alcohol, will be considered in another chapter.

SUMMARY OF THE PHYSIOLOGY OF YEAST.—On reviewing the intricate considerations that cluster around so comparatively simple an organism as the torula, the main facts may be grouped as follows:—1. *There is an organised structure.* 2. *There is a complex chemical composition* in which molecules of organic and mineral substances are associated and interact in a manner of which we know next to nothing. 3. *There are movements* which give rise to phenomena that constitute the life of the torula. These vital phenomena are mainly the three fundamental vital characteristics met with in every organism, viz. *nutrition*, *growth*, with a small degree of *structural differentiation or evolution*, and *reproduction.* These are fundamental vital characteristics found in every organism save the very lowest, *e.g.* protamœba, where there is no sufficient evidence of evolutionary power in its ordinary life-history at all events.

In order that these vital movements may ensue, there must be a free diffusion of water, oxygen, and other food-stuffs into the torula. The physico-chemical forces of the protoplasmic molecules doubtless play an important part, yet here, as in all plants, they cannot bring about the phenomena of life without the *constant* influence of *heat.* The living protoplasm is excitable, and heat is its normal stimulus. But we do not comprehend how it is that the energy of heat, with the physico-chemical forces of the protoplasmic machinery, produce movements that lead to results characteristic of vitality. *To know this secret should require a complete knowledge of heat, molecular forces, and the molecular machinery of protoplasm.*

The torula may be dried like a seed of corn, and preserved for an indefinite period without losing its power of living. In the dried state vitality is dormant. There is *potential* but no *actual* life. When, however, heat and moisture are applied, the torula actually lives, that is, its molecular machinery moves in a way that leads to vital results. The torula may be killed by exposure to a high temperature, such as that of boiling water, or by the influence of such agents as nitric and sulphuric acids. When such is the case, the moisture and gentle heat that under other circumstances led to vital phenomena now induce decomposition of the organism; doubtless because the too powerful heat or the powerful acids destroy the delicate molecular structure of the protoplasm, and render it incapable of those movements that end in nutrition and growth, and capable only of those that lead to a total disintegration of the complex mechanism.

HAIRS OF TRADESCANTIA.

The hairs on the stamens of *Tradescantia virginica* severally consist of a series of morphological units placed end to end (Fig. 5). Each unit is a cell, and is homologous with the entire organism of the torula, but a higher evolution has here taken place. As in the torula, there is a cellulose periplast enclosing a mass of protoplasm (*p*, Fig. 6), but a part of the protoplasm has been differentiated into a spherical vesicle termed a nucleus (*n*). In the fully formed cells in the shaft of the hair, the protoplasm stretches in a thread-like form amidst large vacuoles containing a watery fluid—the cell-sap. In these cells (Fig. 6) a streaming motion of the protoplasm may be witnessed as long as the cells are living. The whole substance of a protoplasmic thread streams in some cases towards, in others from, the mass of protoplasm around the nucleus. On arrival at the cell wall it flattens out like a viscous jelly, and streams along the interior of the envelope. A better exhibition of the physical characters of protoplasm could scarcely be obtained.

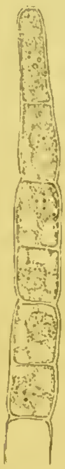

Fig. 5. Hair from stamen of Tradescantia. × 50.

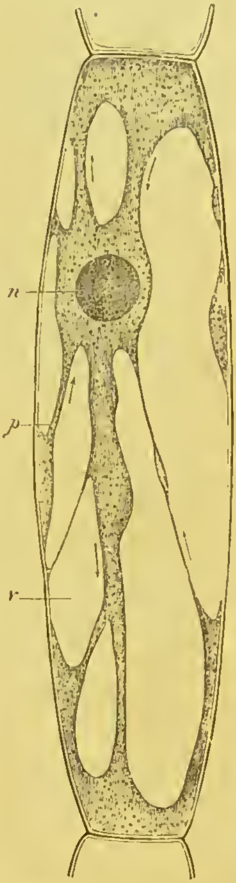

Fig. 6. Cell from hair shown in Fig. 5. *n*, Nucleus; *p*, protoplasm; *r*, vacuole. The arrows indicate the direction of the protoplasmic streams. × 400.

Although we do not comprehend the manner in which the peculiar protoplasmic movement seen in this, and in some other vegetable cells is brought about, it, like muscular movement, is doubtless dependent on chemical changes in the protoplasm. Of these changes we know nothing further than this, that *respiration* is indispensable. In the absence of oxygen the movement soon ceases, and in an atmosphere of carbonic acid it is very easily arrested (Kühne, *Op.* 30, p. 106), but reappears when the carbonic acid is replaced by air.

A gentle heat hastens the movement, doubtless by accelerating chemical change, but if the temperature be raised to 45° C. (113° F.), (Schultze), the movement ceases, the protoplasmic threads contract and break up into rounded masses. This is regarded as a *heat-stiffening*, similar to the rigidity produced in a muscle by heat.

When a shock of induced electricity is transmitted through the living protoplasm, it contracts, somewhat as a muscle does when thus stimulated. The protoplasmic threads shorten, and being soft, break up into rounded masses, and the streaming motions cease, just as happens when the cell is overheated (Kühne). Owing to this change of shape on stimulation, it is inferred that the protoplasm is contractile, and although the streaming movement has not been explained, it probably in some way or other results from contractility (Kühne).

As the cells grow old, the vacuoles enlarge, the protoplasm gradually disappears, and nothing but the cellulose-periplast and cell-sap remain.

AMŒBA.

The protamœba (Fig. 3) is a simple undifferentiated mass of protoplasm. In the amœba (Fig. 8) the protoplasm (*p*) usually encloses a vesicular nucleus (*n*), and this in turn a granule termed a nucleolus (*n'*). The protoplasm may have a uniform finely granular appearance, but in some cases its outer part is hyaline. There is usually no periplast, but sometimes this is produced by the protoplasm, and the amœba thus becomes encysted (*D*).

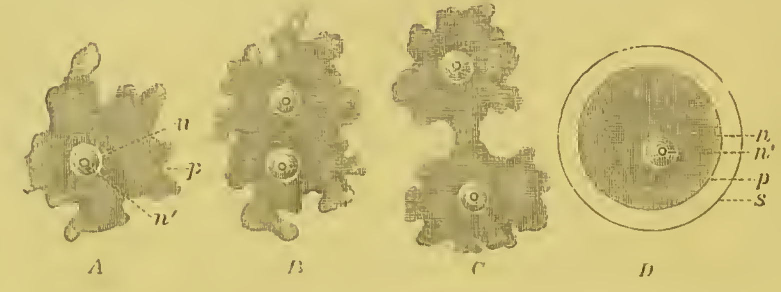

Fig. 7. *A*, Amœba. *B C*, undergoing division. *D*, quiescent amœba encysted : *s*, envelope ; *p*, protoplasm ; *n*, nucleus, *n'*, nucleolus. × about 400. (Hæckel.)

Amœboid Movement.—The protamœba and the non-encysted amœba constantly exhibit in their normal condition a motion termed *amœboid.* This is characterised by *indefinite* changes of shape due to a streaming motion of the protoplasm. Protrusions of the protoplasm (*pseudopodia*) occur at any part of the surface. These may afterwards be withdrawn, or the general mass of the protoplasm may move towards them, and thus a locomotion of a part or of the whole of the amœba ensue. Amœboid movement is ascribed to contractility,—a property belonging to some forms of protoplasm and to some of its modifications, whereby its particles assume different relative positions, and thus occasion an indefinite or definite change of shape in the mass ; thus, when a muscle contracts, the change of shape is always in a *definite* direction, but in amœboid masses of protoplasm the changes of shape are altogether *indefinite.*

The study of amœboid motion is very instructive, for it leads to the conviction that within a *continuous protoplasmic unit, excitement may be partial or general.* A shock of induced electricity sets up a general excitement, the amœba withdrawing its processes and becoming spheroidal. If the shock is not too powerful, the amœba after a time again begins to crawl about, but with shocks of great intensity the contractile substance is paralysed. When the amœba comes into contact with solid particles, it throws out processes around them, and the particles are thus enveloped. It seems as if the protoplasm were *locally* excited by the contact of the particles, nevertheless, processes may be thrown out when the amœba is not in contact with any solid matter.

Cold retards, while a moderate heat accelerates the motion—doubtless by retarding or hastening the metabolism on which the mechanical movement immediately depends. On raising the temperature from 40° to 45° C. (104° to 113° F.) a permanent heat-stiffening ensues, owing to coagulation of the proteid matter of the protoplasm, and death is the result. Similar effects are produced by heat on the contractile substance of muscle. The movements of the amœba must be regarded as resulting from chemical changes within the protoplasmic machinery. An appropriate external stimulus, such as an electrical shock, may induce a sudden discharge of energy, but often the movements occur without any apparent external liberator. It is convenient to apply the term *automatic* to motions that result in protoplasm and its modifications from internal causes. In every case, however, the pabulum needed to supply the protoplasm with energising material must, like the fuel of a steam-engine, necessarily come from without, although, when once the protoplasmic machinery is thrown into the motions that constitute life, the liberation of the energy of the explosive material may result automatically and not from external stimuli.

NUTRITION OF AMŒBA.—The amœba is believed to be an animal, because it never secretes a cellulose periplast, and it cannot integrate protoplasm out of *simple substances* like a plant. Like all other animals it must be supplied with oxygen, proteid and mineral matters, and it may be that—as in most animals—fats and carbohydrates are also required. The amœba obtains its food mostly from vegetable organisms. The animalcule entangles and envelopes them, and extracts their nutrient matter. Probably the proteid materials of the food particles undergo a sort of digestion, and are thus transformed into substances that readily diffuse throughout the amœbal protoplasm to nourish its every part. The food-stuffs are *assimilated* both chemically and physically (p. 20). Much of the assimilated food is doubtless employed for the building up of new protoplasm; a portion of it, possibly a different portion, is, like the fuel of a steam-engine, destined not for *plastic* ends, but for the supply of mechanical energy. At the same time, however, we are unable to say whether the energising material is not at some time or other a part of the protoplasmic framework, or merely exists within its interstices.

The amœba, like every other protoplasmic mass, *respires,*—absorbing oxygen and excreting carbonic acid; the admission of the one and the escape of the other being essential for its vital manifestations. But no doubt carbonic acid is not its only waste matter. Effete azotised substances doubtless result from the *disassimilative* (disintegrative) metabolism of the proteid matter. Of the nature of these we in this instance know nothing, but probably they closely resemble creatin ($C_4 H_9 N_3 O_2$) or creatinin ($C_4 H_7 N_3 O$), effete azotised matters derived from the modified protoplasm of muscle.

REPRODUCTION OF AMŒBA.—Both the protamœba (Fig. 3) and the amœba (Fig. 7) multiply by *fission.* An encircling furrow appears in the protoplasm, gradually deepening until the mass cleaves into two distinct individuals. In the amœba the fission of the protoplasm is preceded by that of the nucleus (Fig. 7, *B C*). The *fissiparous* is by far the most common mode in which the protoplasmic unit multiplies in the plant as well as in the animal. It is one of the most characteristic and remarkable of vital movements. Its determining cause is entirely unknown. In the encysted amœba (Fig. 7, *D*) the cleavage occurs again and again within the periplast, *which takes no share in the production of the new units.*

THE OVUM.

All the tissues of the body are developed from the impregnated ovum.

The ovum is a cell morphologically similar to the encysted amœba (Fig. 7, *D*). It (Fig. 8, *A*) has an envelope or periplast—the *zona pellucida* (*s*); enclosing a mass of protoplasm—the *yelk* (*p*). Within this there is a nucleus—the *germinal vesicle* (*n*), and a nucleolus—the *germinal spot* (*n'*). The protoplasm is peculiar in containing many fatty particles.

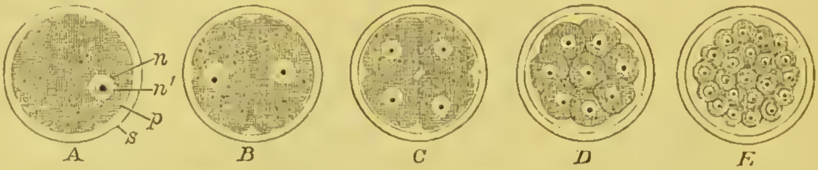

Fig. 8. Diagrams to illustrate (*A*) the structure of the mammalian ovum, and (*B, C, D, E*) the cleavage of its nucleated protoplast. *n*, Nucleus; *n'*, nucleolus; *p*, protoplasm; *s*, periplast. (*Magnified.*)

The ovum is impregnated by one or more spermatozoids penetrating its periplast and mingling with its protoplasm, in which they break down and disappear. This is preceded or immediately followed by a disappearance of the germinal vesicle. The whole protoplasmic mass cleaves into two parts. It is doubtful whether a new nucleus appears previous to cleavage, but usually a nucleus may be seen in each segment (*B*). The nucleus and the protoplasm of each mass divide into two (*C*), and this process is repeated again and again until a vast number of minute nucleated protoplasts are produced (*E*). The periplast of the ovum (*zona pellucida*) remains entirely passive; it has nothing to do with the formation of the new individual, which entirely results from the impregnated protoplasm.

GERMINAL MEMBRANE.—The multitude of nucleated protoplasts resulting from the yelk-cleavage arrange themselves in the form of a membrane —the *germinal membrane*, or *blastoderm*—immediately within the zona pellucida. At first there is a single layer, but it soon divides into two, an outer and an inner, termed respectively the *epiblast* and *hypoblast*. Soon thereafter a third layer—the *mesoblast*—is formed between them, and all three take a share in the production of the tissues of the embryo in a manner to be afterwards described in the chapters on Development.

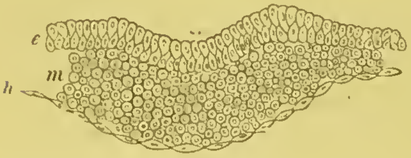

Fig. 9. The three layers of the blastoderm. *e*, Epiblast; *m*, mesoblast; *h*, hypoblast. (Balfour.)

All the tissues are composed of repetitions of the morphological unit —the cell—variously arranged and variously modified. On tracing their development from the germinal membrane it is found that many of the units undergo remarkable differentiations. The units that became white blood-corpuscles remain as nucleated masses of unenveloped protoplasm, exhibiting amœboid movement. Those that become the cells of secreting epithelium also remain usually without a periplast. But although in coarser structure they resemble white blood-corpuscles, they must have undergone some profound physico-chemical differentiation, for they rarely exhibit any amœboid movement, and are the active agents of secretion. Some of them, *e.g.* the epithelial cells of the kidney, have a special attraction for urea, uric acid, and some other effete substances which they withdraw from the blood, and thus act as scavengers in the bodily economy. Others are the seats of an active metabolism for the production of new substances, some of which, *e.g.* the pepsin formed in the gastric glands, discharge important functions; whilst others, *e.g.* the bile-pigments produced in the cells of the liver, are to be thrown out of the organism as useless. In other epithelial cells part of the protoplasm is modified into contractile cilia. In yet other epithelial cells, *e.g.* those covering the skin, the protoplasts produce horny periplasts, which collectively form a pliable but resistent covering for the body, and thus discharge an important mechanical function.

In those units that give rise to connective, cartilaginous, osseous, and dental tissues, the striking differentiation consists in the formation of periplasts, with varying physical and chemical properties. In connective tissue it is mostly a pliable but strongly resisting fibrous tissue. In bone it is a dense and unyielding calcified fibrous tissue, and so on. In all cases *the periplast discharges simply a passive mechanical function,* acting as a delicate packing between various soft tissues, or as strong membranes and cords for the binding of various parts together, or as rigid supports for the soft parts of the body, as in bone.

In the units from which muscle is developed the protoplasm is so differentiated that it becomes elastic, and its contraction is no longer amœboid, but in a definite direction.

In the units that become nerve cells the protoplasm loses its contractile power, but becomes the producer of nerve energy with all its wonderful manifestations. The protoplasm of other nerve units becomes transformed into the delicate fibrils of the nervous threads, that neither exhibit contraction nor evolve nerve energy, but constitute strands of highly excitable tissue that may be thrown into invisible motion by the energy of the nerve cell, or by various other forms of energy, and thus become the means of conveying swift messages between distant parts of the complicated bodily mechanism. Full details, however, regarding the manifold physico-chemical and functional differentiations of the various units of the blastoderm, as they develope into the several tissues, can only be given when the tissues become individually the subject of study. But with regard to the morphology of the several tissue units, it will be found that each unit is either

1. A protoplast—usually nucleated, but sometimes simple—without a periplast, as in the white blood-corpuscles.

2. A protoplast usually nucleated—with a periplast, as may be seen in bone and cartilage.

3. A periplast from which the protoplast and nucleus have vanished, as in the enamel fibres of the teeth, etc. Sometimes, however, the nucleus remains within the periplast.

To these three categories we may refer all the morphological forms of the tissue units met with in complex organisms, and it is to be observed that their prototypes are all to be found in the organisms low in the living scale; thus—1. The protamœba is a simple protoplast. The amœba is a protoplast mostly nucleated and mostly without a periplast. 2. The torula is a simple or a nucleated protoplast, with a periplast. The tradescantia cell is a nucleated protoplast, with a periplast; while 3. The old torula and the old tradescantia cells are periplasts, from which the protoplasts have vanished.

THE CELL THEORY.

Animal histology first passed from seeming chaos into the order of science when Schwann (1838, *Op.* 29) brought it within the domain of the great morphological law, that, however diverse in structure and function the several tissues of organisms may be, "*there is one universal principle for their development, and that principle is the formation of cells*" (*Op.* 29, p. 165). The tissues are composed of cellular units and intercellular substance, each unit having a vitality more or less independent. That is the essence of the cell theory, which was first enunciated by Schleiden with reference to the tissues of plants. When Schwann applied it to animal tissues he had to discharge a far more difficult task than Schleiden, for while the cellular units are readily perceptible in vegetable tissues they are extremely difficult to detect in some of those of animals. Schwann proved the truth of the cell theory as regards the tissues of higher vertebrates only, but subsequent investigations have shown that the cell theory of the development and constitution of organic tissues really possesses the universal character which he assigned to it.

But relying—as Schwann was compelled to do—on technical methods of microscopy of a very primitive character, it is not surprising that he should have fallen into some errors. Thus in maintaining that "cells are formed in a structureless substance '*cytoblastema*' which lies either *around* or in the interior of cells already existing" (*Op.* 29, p. 165), he fell into the error of supposing that cells may arise *de novo*, by a sort of precipitation. To Martin Barry (*Op.* 3, years 1838-39) belongs the credit of having been the first to correct this error, and to maintain that *every cell springs from a pre-existing cell:* all the cells of the body arising by continuous descent from the ovum. This theory of cell descent received support from Goodsir's researches, both in the domain of physiology and of pathology, and is now all but universally accepted.

Schwann defined a cell as consisting of an envelope, cell fluid, and nucleus; the protoplasm of the cell being unknown until Von Mohl afterwards discovered it in the cells of plants. In describing the supposed free development of cells in a cytoblastema, he stated that the nucleus is first formed by the precipitation and coalescence of particles. The substance of the cell-wall is then precipitated around it, and eventually the cell-fluid accumulates between them, owing to imbibition, and to a power of the cell-membrane to chemically alter and secrete certain substances. Thus, although Schwann failed to demonstrate an envelope around the cells of pus and mucus, yet he ascribed the production of the perinuclear matter of a cell to its envelope. Leydig (*Op.* 31) perceived the error, and maintained that the cell membrane is only a condensed outer layer of the cell substance, whose importance is therefore greater than that of its hardened crust, and constitutes the material substratum for vital processes, and that therefore the essential structure of the cellular unit is a mass of cell-substance enclosing a nucleus. Goodsir had already pointed out the division of the nucleus as the first step in cell proliferation, and had named it on this account the *germinal centre* of the cell. Von Mohl discovered protoplasm in the vegetable cells. Remak, perceiving the similarity between this and the perinuclear substance of the animal cell, and, following Leydig, maintained that the essential part of the cellular unit is *a nucleated mass of protoplasm.* Notwithstanding this, however, the presence of an envelope as an essential part of the cellular element was contended for by Virchow (*Op.* 32, p. 12) so late as 1858, and it is to Beale (*Op.* 33) and Max Schultze (*Op.* 14, year 1861, p. 18 ; *Op.* 34) that the credit belongs of having finally brought back histologists to the position adopted by Leydig and Remak.

But it had already been shown by Brücke (*Op.* 41) that the nucleus is not universally present in the morphological unit, for in the cells of fungi it is generally absent. Beale showed that minute particles of protoplasm without nuclei occur in the blood. Schultze discovered a non-nucleated variety of amœba (*Amœba porrecta*), and Hæckel found a non-nucleated protista—the *Protogenes primordialis.* It was therefore proposed by Hæckel, that as a nucleated mass of protoplasm had been termed a *cell* by Schultze, a non-nucleated mass should be termed a *cytode.* At first glance this nomenclature appears advantageous. Thus the protamœba is a cytode, the ordinary amœba a cell, the torula a cytode with an envelope, and the ovum a cell with an envelope ; but we are landed in difficulty with such cases as the old vegetable cell from which the protoplasm has disappeared ; the enamel fibres of the teeth, which were at first cells, but have become rods of calcified material without nucleus or protoplasm ; the coloured corpuscles of lower vertebrates, which have a nucleus and cell-membrane, but whose protoplasm has given place to a pigment ; and the mammalian coloured blood-corpuscle, where both nucleus and protoplasm have vanished. Yet, although to none of these cases are the terms cytode, and cell in its restricted sense, applicable, they are all well-defined morphological units, in which peculiar developments have occurred. In consequence of the confusion introduced by this change in the significance of the term cell, it has been proposed to abandon it, and to substitute the word *corpuscle*, but as this term is too vague, and as the word cell is classical, it is still, and will probably always be, generally employed. The imperfection of the proposed nomenclature lies in its ignoring the periplast of the morphological unit. Thus the old torula, the enamel fibre, the mammalian red blood-corpuscle, although they cannot be described as *cell-envelopes*, and still less as *intercellular substance*, may nevertheless be correctly termed *periplasts ;* that is to say, they are morphological units in which a protoplast—cytode or cell—once existed, but has now produced and given place to a periplast. The red blood-corpuscle of lower vertebrates is a nucleated periplast ; that is, there is a nucleus and a periplast, but no protoplasm.

We might therefore indicate the chief varieties of the morphological unit by designating them either—

1. A cytode—simple or with a periplast.
2. A cell „ „ „
3. A periplast.

Or, we may designate them—

1. A simple protoplast, with or without a periplast.
2. A nucleated protoplast „ „ „
3. A periplast.

We prefer the latter nomenclature because it allows us to use the classical term *cell* in a general sense, as indicating the morphological unit; although it must be admitted that it is sometimes, *e.g.* in the case of cartilage, convenient to apply the term to only a part of the cellular unit—the nucleated protoplast.

It has been already indicated that protoplasm is in evolution the primary and fundamental part of the morphological unit; the protamœba consists of nothing else. The *nucleus*, however, is so generally present that it demands a careful scrutiny. In young cells it is mostly spherical, but as age advances it may become oval or spindle-shaped. In some cases it presents a single contour, and appears to be solid, while in others its double contour indicates a vesicular character. Within the vesicle there is a fluid, and it has recently been shown by Flemming, Klein (*Op.* 8, vol. xv. p. 315), and others that in many nuclei there is a network of very fine fibrils. The nucleus of some cells, at all events—*e.g.* pus-cells and blood-corpuscles—contains an albuminoid substance termed nuclein. The nucleus has a stronger affinity than protoplasm for such dyes as carmine and magenta; but, unlike protoplasm, it is not readily affected by alkalies and acetic acid. And yet, though physically and chemically different from protoplasm, we have seen that it behaves similarly when the cell multiplies by cleavage, and, indeed, it often divides completely before the surrounding protoplasm has even become furrowed. This power of germinating suggests that the nucleus must be regarded as a near modification of protoplasm, and Beale[1] was led by this consideration to embrace the nucleus and protoplasm under one common term—*germinal matter*. The almost universal presence of the nucleus suggests that it possesses some important function, of which, however, nothing is definitely known. That of the *nucleolus* is equally obscure. In some cases it is absent; in others one, two, three, or more may be present. The chemical nature of the nucleolus is quite unknown.

As regards the periplast of the cellular unit, it must be specially remembered that the term periplast, unlike the term protoplasm, indicates *nothing regarding the structural nature* of the parts to which it is applied, for it is applicable to the matrix of cartilage and bone, the sheath of muscular fibre, and the fibres of connective tissue. It merely indicates a *genetic relation*, and implies that it is that part of the morphological unit which has been produced by the protoplast, simple or nucleated. Although its chemical and physical characters are most varied, and although it may, as in the matrix of cartilage, undergo very marked physical and chemical changes, it—unlike the protoplast—*never proliferates and produces new units.*

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[1] The views of Beale, according to which he groups the parts of the morphological unit into *germinal matter* and *formed material*, cannot be discussed until the structure of the elementary tissues is detailed. It ought, however, to be stated here, that what we term *periplast* is not always applied to what Beale terms "formed material." Neither do we use the term *protoplasm* as synonymous with "germinal matter."

Cell Multiplication.—The simplest mode in which cells multiply is by *gemmation*. We have already studied the process in the torula, and it is sufficient to add that in cells where the protoplasm is nucleated, the bud simply grows from the outer part of the protoplasm without any apparent participation of the nucleus in the process. But in the higher plants and animals gemmation is rare; the common mode of cell multiplication being *fission*. As this process has been already described in the protamœba, amœba, and ovum, it is sufficient to observe that as regards the division of the protoplasm the process is similar in the presence or absence of the nucleus, but when the nucleus is present it divides before the protoplasm, and when the protoplast is enveloped in a periplast, the division of the former does not implicate the latter.

In the ovum the fission of the protoplast occurs rapidly, and the periplasts secreted around some of the protoplasts have no connection with the original periplast—the *Zona pellucida*. But in the case of hyaline cartilage, where the cell-division usually takes place slowly, a new periplast is formed around each of the new protoplasts. The two layers of the periplast between the apposed surfaces of the protoplasts (Fig. 39) form a septum, which has been erroneously supposed to grow inwards from the original periplast. But it may happen that the cartilage protoplast proliferates rapidly, and a brood of young cells is enclosed within the original periplast, giving rise (Fig. 41) to an appearance not unlike that of the ovum during segmentation. The term *endogenous* is sometimes applied to this variety of the fissiparous mode. There are, therefore, only two essentially different modes in which the cell proliferates—1, the *gemmiparous*; 2, the *fissiparous*—the endogenous mode being only a variety of the second of these.

As long as Schwann's doctrine of the free formation of cells in a cytoblastema outside other cells was believed, the term *exogenous* was employed to distinguish this mode. But as the production of cells in this manner is no longer generally credited, the term has become obsolete.

CHAPTER V.

THE GENERAL CHEMISTRY OF THE BODY.

As it is impossible for the student to learn fully what is known of the chemistry of the body until the whole subject of nutrition has been studied in detail, it is proposed to give in this chapter merely such a *general outline* of the subject as will enable him to comprehend the chemistry and nutrition of the simple tissues.

THE FOOD AND THE EXCRETA.

The nutrition of the organism requires the introduction of suitable quantities of (1) One or more proteids, *e.g.* albumin; (2) One or more carbohydrates, *e.g.* sugar or starch; (3) Fat; (4) Mineral solids, such as alkaline chlorides, sulphates, and phosphates, earthy phosphates, and iron; (5) Water; (6) Oxygen. Life could indeed be maintained without the carbohydrates and fats, for they are to some extent formed from proteids within the economy, but, for reasons to be afterwards given, nutrition becomes unhealthy when they are omitted from the food. The composition of all save the azotised articles of diet—the proteids—is known. These contain C H N O S in quantities that are unknown, but it is certain that their molecules are extremely complex.

In the alimentary canal, the proteids and some of the carbohydrates are variously changed by the influence of ferments in the digestive juices. The food molecules enter the blood, some being absorbed into the blood-capillaries of the stomach and intestines, and passing from thence through the portal vein and liver into the general circulation; while others, especially the fats, pass into the lymph-capillaries and through the thoracic duct reach the blood. In the blood and lymph the food molecules are conveyed to all the tissues. Assimilation and disassimilation, with all the manifold and obscure molecular transformations implied in these processes, occur. The effete matters re-enter the blood, and are removed therefrom by the organs of excretion—the lungs, skin, liver, and kidneys. In passing through the economy the complex organic molecules are to a large extent disintegrated into effete substances, of which urea ($C\ H_4\ N_2\ O$), uric acid ($C_5\ H_4\ N_4\ O_3$), creatinin ($C_4\ H_7\ NO_3$), cholesterin ($C_{26}\ H_{44}\ O$), carbonic, sulphuric, and phosphoric acids, are the most important. Although some of these effete matters have a composition by no means simple, they nevertheless form a striking contrast to those matters from whose regressive metamorphosis they are derived. Yet, although many of the intermediate stages in the metabolism of the molecules of the food into those of the tissues, and finally into those of the excreta, are known, it must be admitted that our present knowledge of the whole subject is so meagre that we are as yet scarcely within its threshold.

THE GENERAL CHEMICAL COMPOSITION OF THE BODY.

What is known of the composition of organisms has been ascertained by *ultimate* and by *proximate* analysis. By ultimate analysis the chemist seeks to resolve the body into its *ultimate or elementary principles,* while by proximate analysis he endeavours to ascertain as nearly as possible what chemical compounds really exist in the body. Thus he isolates from the blood, albumin, sodium chloride, water, etc.; and believing that these substances really exist as such in the fluid, and are not produced by the processes employed, he regards them as *proximate principles.* Owing to the roughness of such a process as the ignition of an organic substance, compound principles are obtained which may not be *proximate* principles. Thus sulphuric, phosphoric, and carbonic acids are actually produced in the combustion of an organism, and could not therefore be regarded as its *proximate principles,* unless some other method of analysis, free from fallacy, proved them to be such. Although much has in this way been ascertained as to the proximate principles of the *dead* body, our knowledge of the proximate principles of the *living* organism is still very fragmentary; for many, especially the azotised substances, are extremely unstable, and are apt to change, not only in the hands of the chemist, but in the act of death, which in nearly every instance must have occurred ere his processes are applied. Thus fibrin is readily separable from the blood at death, and was formerly believed to be a *proximate principle* of the blood during life; but it is now known that it results from the union of two separate compounds which in the present state of our knowledge are regarded as proximate principles. *The very fragmentary character of our knowledge regarding the real proximate principles of the living body must be carefully borne in mind.*

ULTIMATE PRINCIPLES.—Only fifteen chemical elements are constantly found in the body. Of these nine are non-metals—carbon, hydrogen, nitrogen, oxygen, sulphur, phosphorus, chlorine, fluorine, and silicon; while six are metals—sodium, potassium, calcium, magnesium, iron, and manganese. Copper, lead, and lithium are occasionally present. All these elements are found in various states of combination, but part of the oxygen, nitrogen, and hydrogen occurs in a free state.

Free oxygen enters the blood by the lungs, and is carried to all parts of the body to oxidise organic compounds. Although most of it is either loosely or firmly combined, some of it exists in a free state in the blood and other fluids.

Free nitrogen—mostly absorbed from the atmosphere—occurs in the blood and other fluids in small amount. Free hydrogen is found in the alimentary canal, where it is liberated from its compounds, probably during butyric acid fermentation.

PROXIMATE PRINCIPLES.—The chemical compounds found in all organisms may be broadly divided into two great groups, the *mineral* and the *organic*. This division, although somewhat arbitrary, is convenient. *Mineral* or inorganic substances are those which are *most commonly* formed in the inorganic world, and which are scarcely at all produced in living beings; while *organic* substances are those whose natural seat of formation is in organisms, although many of them may also be produced artificially. Every solid and fluid of the body contains both mineral and organic substances, whose relative proportions vary in different cases.

MINERAL COMPOUNDS.

The inorganic substances are water, mineral acids, mineral bases, and mineral salts.

Water is the chief mineral constituent, forming about 70 per cent of the weight of the body.

Hydrochloric Acid.—Free in the gastric juice, but elsewhere combined with the alkalies, as chlorides of sodium, potassium, and ammonium. The last is rare; the first is the most common, and it exists very generally throughout the body. *Sodium Chloride is by far the most abundant mineral salt in the body.*

Sulphuric Acid, combined with sodium and potassium, is found in most of the tissues and fluids.

Phosphoric Acid (common, tribasic, or orthophosphoric acid), combined with sodium, potassium, lime, and magnesium, is found in all the tissues and fluids, calcium phosphate being especially abundant in bone and tooth. Phosphoric acid also enters into the composition of lecithin, a complex azotised fat largely found in nerve tissue.

Iron forms a part of a complex organic body, the blood-pigment. *fluoride of calcium* is found in the bones and teeth, while *manganese* occurs in traces in various parts.

Sources of the Minerals.—The free hydrochloric acid of the gastric juice is derived within the body from chlorides. Small quantities of water, sulphuric and phosphoric acids, are produced by the oxidation of the H. S. and P. of organic compounds; but the great bulk of these substances, with all the other mineral matters, enter the body from without.

The *functions* of the mineral substances are very imperfectly known. *Water* is the general solvent for the various solids and gases, and gives a soft consistence to various parts. *Sodium chloride* is necessary for the solution of the globulin family of proteids; thus without its presence in small amount, the contractile substance of muscle—a globulin—would become solid. *Earthy salts* give hardness to the bones and teeth. The *sodium* phosphate of the blood and lymph is one of the carriers of carbonic acid from the tissues to the lungs. All these substances, however, have probably other important functions. *Hydrochloric acid* plays an important part in the digestion of proteids.

As water and mineral solids are found in every organism, however simple, their functions, although so imperfectly known, must be held to be as essential in the organic fabric as the so-called organic matter. Yet, however important they are in establishing certain physical conditions, and however essential may be their chemical relations, this holds true of them all, *they are not sources of bodily energy.* This springs from organic substances only, by oxidation and otherwise.

ORGANIC COMPOUNDS.[1]

The organic compounds might be classified as azotised and non-azotised, but as such a classification leads to difficulties, we may group them as follows:—I. Proteids and their allied Principles. II. Azotised Derivatives of the Regressive Metabolism of I. III. Carbohydrates. IV. Alcohols. V. Fats and their Allies.

I. PROTEIDS AND THEIR ALLIES.

Proteids and their allies constitute the chief solids of the blood and lymph, and of all the tissues excepting the bones and teeth. They have all an exceedingly complex composition, that in most instances is not definitely ascertained. Most of them, especially the proteids, are very unstable, and readily decompose into a number of simpler bodies. Some of them are in intimate relation with salts, bases, and acids, from which they cannot be detached without undergoing change. They are mostly amorphous.

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[1] It is not intended in this chapter to give anything like a detailed account of the reactions of the proximate principles. These will be fully given in an Appendix; and in the chapters on the Tissues and on Nutrition, details will be given that would here prove uninteresting and distracting.

A. Proteids.

The chief members of this group are—1. Albumins. 2. Globulins. 3. Fibrin. 4. Alkali-albumins. 5. Acid-albumins. 6. Peptones.

These substances were termed proteids by Mulder, on the theory that they are all compounds of a primary principle—*protein.* Although this theory is now discarded, the term proteid is retained for convenience. Their percentage composition in 100 parts is—

	C.	H.	N.	O.	S.
From . .	52·7	6·9	15·4	20·9	0·8
To . .	54·5	7·3	16·5	23·5	2·0

Their molecular weight and constitution are unknown.

1. *Albumins.*—Albumin is the chief organic constituent of the transparent part of an egg, and of the serum of the blood. As the albumins derived from these two sources are slightly different, they are distinguished as *egg-albumin* and *serum-albumin.*

Albumin from either of these sources is soluble in water. When its solution is evaporated at a low temperature, a transparent residue remains, which can be easily redissolved. As it scarcely at all diffuses through animal membrane, it is a characteristic colloid. Its solution turns a polarised ray towards the left.

When a solution of albumin is heated to from 60° to 70° C. (140°-158° F.) it coagulates. The presence of water is necessary for this change; for if the albumin be previously dried, it *may be heated to the temperature of boiling water without* undergoing change. The previous addition of very dilute acetic or phosphoric acid to an albuminous solution lowers the temperature at which coagulation occurs. On the other hand, the addition of a very little alkali—*e.g.* sodium carbonate—raises the temperature of coagulation, and if the alkali be in excess, coagulation is altogether prevented.

Albumin is not precipitated by carbonic, acetic, tartaric, or mineral acids, if these be dilute and added in very small quantity; but if added in excess, precipitation occurs. Nitric acid is the most powerful precipitating agent. The precipitate thrown down by nitric acid is *soluble in excess in the case of serum-albumin,* but scarcely at all in that of egg-albumin. Albumin is also precipitated by tannic acid, alcohol, and by most of the salts of the heavy metals, such as mercuric chloride.

Although the chemical difference between egg-albumin and serum-albumin is not striking from their reactions, there is nevertheless a great physiological difference between them, for if egg-albumin be introduced directly into the blood or lymph vessels, it is largely excreted by the kidneys as a foreign substance (Bernard).

2. *Globulins* are found in the blood, chyle, and lymph, in muscle, and in protoplasm generally. They are closely allied to albumin, but, unlike albumin, they are not soluble in pure water. They are, however, readily

soluble in water containing a little sodium chloride (1 per cent), but the addition of an excess of the salt precipitates them. The addition of any amount of salt to a fluid containing *albumin* occasions no precipitate. In other respects they resemble albumin. The substances belonging to the globulin group are :—*a. Crystallin*, or *globulin* proper, derived from the crystalline lens. *b. Fibrinoplastin*, or *paraglobulin*. *c. Fibrinogen.* Both *b* and *c* are found in the blood, chyle, and lymph. *d. Myosin*, the chief constituent of muscle, and a constituent of protoplasm generally (Hoppe-Seyler, *Op.* 28, p. 76).

3. *Fibrin* is not found in the living body, but appears when blood, lymph, and chyle coagulate. It results from the union of the two globulins, fibrinoplastin and fibrinogen. It is insoluble in water, solutions of salt, and dilute acids. When heated it assumes the properties of coagulated albumin.

4. *Alkali-Albumins* or *Albuminates.*—All the albumins and globulins, when added to solutions of caustic alkali, form compounds termed alkali-albumins or albuminates. *Casein*, the chief proteid constituent of milk, is believed to be a potassium-albumin, but it is not identical with potassium-albumin produced artificially. Casein is not coagulated by heat unless an acid be previously added.

Acid-albumin or *Syntonin* does not exist in the body, but results from the action of dilute acid (*e.g.* 0·2 per cent HCl) upon the proteid substances already mentioned.

5. *Peptones.*—All the above proteids, when subjected to the influence of the hydrolytic ferments of the gastric and pancreatic juices, are converted into peptones. Peptones are soluble in water, and, unlike the solutions of other proteids, *are diffusible.* By this means the proteids are enabled to diffuse from the alimentary canal into the blood-vessels. The albumin of the blood is derived from peptones, by some process the reverse of that by which they are formed in the alimentary canal. Unlike albumin, peptones are not coagulated by heat and mineral acids, but, like albumin, they are precipitated by tannic acid, mercuric chloride, and by an excess of alcohol.

The following chemical reactions are common to all the proteids :—

a. They are all soluble in caustic alkalies.

b. After the previous addition of weak acetic acid to their solutions they are precipitated by potassium ferrocyanide.

c. On the addition of a trace of cupric sulphate, followed by a solution of caustic potash, a violet colour appears, which becomes deeper on boiling.

d. If their solutions be boiled after the addition of strong nitric acid they assume a yellowish colour, which becomes bright orange or amber on adding ammonia (Xanthoproteic reaction).

B. Albuminoids.

The albuminoids are closely related to the proteids, and are either produced from proteids alone or from these with other substances by the vital influence of cells, but by what special processes is altogether unknown. Like the proteids, they are amorphous, and resemble them in general composition, but unlike the proteids, some of them contain no sulphur. *They are not converted into peptones by the gastric and pancreatic ferments*, although, like proteids, they yield leucin and tyrosin ; sometimes the one, sometimes the other, or both, when subjected to hydrolytic treatment. In other respects the members of the group have no common characters, and differ widely amongst themselves.

1. *Mucin* (C 52·2, H 7·0, N 12·6, O 28·2 per cent) occurs in mucus and in mucous tissue, and is the cause of their viscidity.

2. *Gelatin* or glutin (C 50·4, H 6·8, N 18·3, S + O 24·5 per cent) is obtained by the prolonged boiling of white fibrous tissue and of the organic substance of bone. As gelatin swells up but is not soluble in cold water, and as white fibrous tissue does not swell up in cold water, it is believed that gelatin does not exist as such in the tissue, but that it is derived from a hypothetical principle—*collagen.*

3. *Chondrin* (C 49·9, H 6·6, N 14·5, S 0·4, O 28·6 per cent) is obtained by the prolonged boiling of hyaline cartilage. It is supposed to be derived from a hypothetical principle—chondrogen.

4. *Keratin* (C 50·3-52·5, H 6·4-7, N 16·2-17·7, S 0·7-5, O 20·7-25 per cent) is the chief constituent of hair, horn, nail, and other epidermic tissues.

5. *Elastin* (C 55·5, H 7·4, N 16·7, O 20·5 per cent) is the principal constituent of elastic tissue.

Mucin swells up but does not perfectly dissolve in water. The presence of a little sodium chloride increases its solubility. It is readily precipitated by alcohol and by acetic acid; the precipitate is not dissolved by sodium sulphate.

Chondrin is soluble in hot but not in cold water, is precipitated by acetic acid, and the precipitate is dissolved by sodium sulphate.

Gelatin swells up, but does not dissolve in cold water. It dissolves in hot water, and forms a jelly on cooling. It is not precipitated by acetic acid, nor by acetic acid and potassium ferrocyanide, like the proteids.

Keratin is insoluble in water—cold or hot. It is only soluble in hot solutions of the alkalies.

Elastin is an exceedingly insoluble substance. It is dissolved by prolonged boiling in caustic potash, but, unlike keratin, is decomposed thereby.

6. *Ferments* that convert starch and glycogen into glucose (*amylolytic*), proteids into peptones (*proteolytic*), and break up fats into glycerin and fatty acids (*fat-decomposing*), occur in the body. All of them are hydrolytic, and will be afterwards referred to in detail.

C. Substances more complex than Proteids.

Although the synthesis of proteids from their elements does not occur in the animal body, yet to a slight extent there is the power of raising proteids to a more complex composition. At present three substances are known which occupy this position.

1. *Hæmoglobin*—a crystalline substance (the colouring matter of the blood-corpuscles)—is the most complex substance known. The following formula is given by Preyer—$C_{600} H_{960} N_{154} Fe S_3 O_{179}$. It may be decomposed into a great number of bodies, amongst which a proteid (*globin*) and a pigment (*hæmatin*) are the most notable. It will be fully studied with the composition of the blood.

2. *Vitellin* is abundantly found in yolk of egg, and also in protoplasm generally (Hoppe-Seyler, *Op.* 28, p. 77). It is a crystalline substance, and may be decomposed into a proteid and a phosphorised fat (*lecithin*).

3. *Nuclein* ($C_{29} H_{49} N_9 P_3 O_{22}$) has been obtained from the nuclei of pus-corpuscles

(Miescher) blood-corpuscles, from spermatozoids, and from the cells of yeast (p. 19). It somewhat resembles mucin, but, unlike that substance, contains phosphorus.

II. AZOTISED DERIVATIVES OF THE REGRESSIVE METABOLISM OF PROTEIDS AND THEIR ALLIES.

Ammonia and Ammoniacal Derivatives.

1. AMMONIA and ammoniacal salts occur in small quantity in the blood and other parts.

2. COMPOUND AMMONIAS OR AMINES are bodies in which the hydrogen atoms of ammonia are replaced by hydro-carbon molecules. None of them have been found within the organism, but may be obtained by artificial decomposition. Thus *methylamine* $NH_2\,(CH_3)$ and *trimethylamine* $N\,(CH_3)_3$ may be obtained by the decomposition of creatin, $C_4\,H_9\,N_3\,O_2$.

3. AMIDES are substances in which the hydroxyl group (OH) in acids is replaced by amidogen (NH_2). *Urea* is the biamide of carbonic acid, $CO\,(NH_2)_2$—that is, the hydroxyl (OH) groups of carbonic acid, $CO\,(OH)_2$, are replaced by two molecules of amidogen (NH_2). Urea is excreted by the kidneys, and is the *great azotised derivative* of the proteids and their allies, but it has never yet been obtained from them by artificial means.

4. AMIDO-ACIDS are acids in which hydrogen atoms of the acid radicle are replaced by amidogen (NH_2). Thus:—

$C_2\,H_3\,O\,(O\,H)$	$C_2\,H_2\,(N\,H_2)\,O\,(O\,H)$
Acetic acid.	Amido-acetic acid or glycocin.

The amido-acids may behave as acids or as bases.

a. Glycocin or *glycocoll*, $C_2\,H_5\,N\,O_2$, or amido-acetic acid, does not occur free in the body, but is found combined with cholic acid as *glyco-cholic* acid ($C_{26}\,H_{43}\,N\,O_6$) in the bile, and in relation to benzoic acid, as glyco-benzoic or *hippuric acid* ($C_9\,H_9\,N\,O_3$) in the urine.

b. Taurin, $C_2\,H_7\,N\,SO_3$, is amido-ethyl-sulphonic acid, in which a hydrogen atom of ethyl-sulphonic acid is replaced by a molecule of amidogen ($N\,H_2$). Thus:—

$SO_2\,(O\,H)\,H$	$SO_2\,(O\,H)\,(C_2\,H_5)$	$SO_2\,(O\,H)\,(C_2\,H_4\,[N\,H_2])$
Sulphurous acid.	Ethyl-sulphonic acid.	Amido-ethyl-sulphonic acid.

It is found free in some glandular organs, and is combined with cholic acid, as tauro-cholic acid ($C_{26}\,H_{45}\,N\,SO_7$) in the bile.

c. Leucin is amido-caproic acid, in which one H atom of caproic acid is replaced by a molecule of amidogen ($N\,H_2$). Thus:—

$C_6\,H_{11}\,O\,(O\,H)$	$C_6\,H_{10}\,(N\,H_2)\,O\,(O\,H)$
Caproic acid.	Amido-caproic acid.

d. Tyrosin—$C_9\,H_{11}\,NO_3$—is an amido-acid of unknown constitution.

Leucin and tyrosin usually occur together in various glands. They are readily produced from proteids by the prolonged influence of the proteolytic ferment of the pancreatic juice, and they may also be obtained from proteids artificially.

e. Cystin is found in the kidneys, and sometimes forms urinary calculi; its formula is probably $C_3\,H_5\,N\,SO_2$ (Gamgee and Dewar, *Op.* 1, V. p. 142).

5. AMIDO-ACIDS—IN WHICH THE HYDROGEN OF THE AMIDOGEN GROUPS IS ITSELF SUBSTITUTED.—*a. Sarcosin*, $C_3\,H_7\,NO_2$, is obtained by boiling creatin with baryta water, and is methyl-amido-acetic acid. Thus:—

$C_2\,H_2\,(N\,H_2)\,O\,(O\,H)$	$C_2\,H_2\,(N\,H\,[C\,H_3])\,O\,(O\,H)$
Amido-acetic acid.	Methyl-amido-acetic acid.

b. Creatin, $C_4\,H_9\,N_3\,O_2$, is found in the muscles, blood, brain, etc. By boiling with baryta water, creatin is resolved into sarcosin and urea. By the action of mercuric oxide on an aqueous solution of creatin, methyl-guanidin and oxalic acid are obtained. As the latter is derived from the oxidation of acetic acid, creatin is regarded as methyl-guanidin-acetic acid. Thus:—

$C\,(N\,H)\left\{\begin{matrix}N\,H_2\\N\,H_2\end{matrix}\right.$	$C\,(N\,H)\left\{\begin{matrix}N\,H\,(C\,H_3)\\N\,H_2\end{matrix}\right.$	$C\,(N\,H)\left\{\begin{matrix}N\,H\,(C\,H_3)\\N\,H\,(C_2\,H_2\,O\,(O\,H)\end{matrix}\right.$
Guanidin.	Methyl-guanidin.	Methyl-guanidin-acetic acid.

6. AMMONIACAL DERIVATIVES OF UNKNOWN CONSTITUTION.

a. Uric acid,	$C_5 H_4 N_4 O_3$.	Found in urine, liver, blood, etc.
b. Xanthin,	$C_5 H_4 N_4 O_2$.	Found in urine, liver, blood, etc.
c. Hypoxanthin,	$C_5 H_4 N_4 O$.	Found in muscle, liver, blood, etc.
d. Creatinin,	$C_4 H_7 N_3 O$.	Found in urine and muscle.
e. Allantoin,	$C_4 H_6 N_4 O_3$.	Found in urine.
f. Carnin,	$C_7 H_8 N_4 O_3$.	Found in extract of meat.
g. Guanin,	$C_5 H_5 N_5 O$.	Found in the liver and pancreas.
h. Inosinic acid,	$C_5 H_8 N_2 O_6$.	Found in muscle.

7. CERTAIN PIGMENTS.

a. Bilirubin,	$C_{16} H_{18} N_2 O_3$.	Found in bile.
b. Biliverdin,	$C_{16} H_{20} N_2 O_5$.	,, ,,
c. Hydrobilirubin, or *Urobilin,*	$C_{32} H_{40} N_4 O_7$.	Found in fæces; sometimes in urine.
d. Urochrome,	?	Found in urine.
c. Indican,	$C_{52} H_{62} N_2 O_{34}$.	,, ,,

f. Melanin. Found in the skin and in the eye. It contains C H N O, but its composition is unknown.

The pigments of the bile and urine are probably derived from the blood-pigment—hæmoglobin—a substance having a far more complex composition than any of them.

Substances derived from the Decomposition of Proteids by Artificial Means and by Putrefactive Decomposition.

The following facts regarding the results of the decomposition of proteids by artificial means and by putrefactive ferments are important as showing that the azotised derivatives are in many cases similar to those already detailed as formed in the body, and further because they prove that *fats* may also be derived from the decomposition of proteids.

DECOMPOSITION OF THE PROTEIDS.—*a. By Heat.*—When subjected to destructive distillation the proteids yield an oily fluid, containing (1) Ammoniacal salts of the fatty acids, such as ammonium caproate, butyrate, acetate, and carbonate, and a number of amines—homologous derivatives of the series of ordinary alcohols, such as methylamine, propylamine, butylamine. (2) Bodies belonging to the aromatic group, as aniline and picoline. (3) Phenol, benzol, and their homologues.

b. By Oxidation.—By the action of oxidising agents, as potassium-bichromate with sulphuric acid, etc., there appear bodies belonging to the aromatic and fatty groups, as acetic, benzoic, propionic, valerianic aldehydes; acetic, benzoic, hydrocyanic, propionic, and valerianic acids.

c. By Caustic Alkalies.—When heated with caustic alkali, proteid substances yield leucin, tyrosin, salts of fatty acids, etc.

d. By Mineral Acids.—When boiled with sulphuric and hydrochloric acids, they yield glycocin, leucin, tyrosin, etc.

e. By Putrefactive Ferments.—Putrefactive fermentation is due to the destruction of proteids and some of their allies by living *bacteria*—vegetable organisms that will be afterwards described. Their mode of action is unknown, but probably it largely depends on their robbing the proteids of oxygen. Formic, acetic, butyric, valerianic, caproic, and lactic acids appear, combined with ammonia or other organic alkalies. Some of the nitrogen is eliminated in a free state, but most of it is contained in the ammonia produced. Leucin and tyrosin, sulphuretted hydrogen, carbonic acid, and various other substances, are produced. When the proteids are entirely decomposed by putrefactive fermentation, there remains a substance rich in fats, in earthy and ammoniacal salts, phosphates, and nitrates.

Thus we see in the decomposition of proteids by *a*, *b*, *c*, *d*, the results of the crude and violent processes of the laboratory; whereas under *e*, decomposition, leading in many instances to similar results, can be effected by the subtle influence of the protoplasm of certain minute organisms. It is therefore easy to transfer the thought to the cells of the bodily organism, and to picture them as minute protoplasmic laboratories, effecting varied transformations of proteids and other substances, the proteids yielding not only azotised derivations but also *fats* and other bodies. That fats *are* really derived from them—*e.g.* in the cells of the mammary gland—there is no doubt.

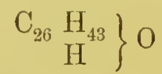
III. CARBOHYDRATES.

The carbohydrates of the body are—(1) *Glycogen* or *animal starch*, $C_6 H_{10} O_5$, occurring largely in the liver, and in most fœtal tissues ; it is also a constituent of muscle and of all amœboid protoplasm. It is chiefly formed from grape-sugar, but may also be derived from proteid substances. It is readily converted into grape-sugar by ferments in the saliva, pancreatic juice, liver, etc. (2) *Grape-sugar*, *dextrose* or *glucose*, $C_6 H_{12} O_6 + H_2 O$. All the starch and cane-sugar of the food are converted by digestive ferments into grape-sugar, most of which passes into the portal vein to the liver, where it is transformed into glycogen. It occurs in small quantities in the blood, lymph, chyle, and muscles. When acted on by yeast it undergoes *alcoholic fermentation*, and under the influence of the *Bacterium lactis* it, like milk-sugar, undergoes *lactic acid fermentation.* (3) *Milk-sugar* or *lactose*, $C_{12} H_{22} O_{11} + H_2 O$, is the only sugar in milk. (4) *Muscle-sugar* or *inosite*, $C_6 H_{12} O_6 + 2H_2 O$, is found in muscle, brain, spleen, etc. The carbohydrates are to a large extent derived from the carbohydrates of the food ; but that they are also produced from proteids has been already stated with regard to glycogen, and will be shown also to hold true regarding the formation of milk-sugar in the protoplasts of the mammary gland. The carbohydrates serve important ends in nutrition.

IV. ALCOHOLS.

1. *Cholesterin*—a monatomic alcohol, $C_{26} H_{43} (OH)$

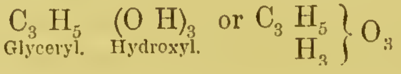
or



$$\left.\begin{matrix} C_{26} H_{43} \\ H \end{matrix}\right\} O$$

is the only free alcohol in the body. It is found in pus cells, white and red blood-corpuscles, the cells of yeast (Hoppe-Seyler, *Op.* 28, p. 79), blood-serum, and largely in the white matter of the brain, spinal cord, and nerves. It is an effete product, and is withdrawn from the blood by the liver, and excreted in the bile. Nothing is known of its source, but the fact of its occurrence in yeast-cells and white blood-corpuscles shows that in these cases, at all events, it probably arises from protoplasmic metabolism.

2. *Glycerin* is a triatomic alcohol, consisting of a radicle glyceryl with three hydroxyl groups ; thus :



$$\underset{\text{Glyceryl.}}{C_3 H_5} \quad \underset{\text{Hydroxyl.}}{(O H)_3} \quad \text{or} \quad \left.\begin{matrix} C_3 H_5 \\ H_3 \end{matrix}\right\} O_3$$

Glycerin probably always occurs in combination within the body. The neutral fats are formed by substituting fatty acids for the H atoms of its hydroxyl.

V. Fats and their Allies.

1. Fatty Acids.—The chief fatty acids found in the body are—

Formic	acid,	$C\ H\ O\ (O\ H)$
Acetic	„	$C_2\ H_3\ O\ (O\ H)$
Propionic	„	$C_3\ H_5\ O\ (O\ H)$
Butyric	„	$C_4\ H_7\ O\ (O\ H)$
Caproic	„	$C_6\ H_{11}\ O\ (O\ H)$
Caprylic	„	$C_8\ H_{15}\ O\ (O\ H)$
Capric	„	$C_{10}\ H_{19}\ O\ (O\ H)$
Palmitic	„	$C_{16}\ H_{31}\ O\ (O\ H)$
Stearic	„	$C_{18}\ H_{35}\ O\ (O\ H)$

These belong to the *acetic acid series.* Oleic acid, $C_{18}\ H_{33}\ O\ (O\ H)$, belonging to the *oleic* acid series, is also present. The fatty acids rarely occur in a free state, although their glycerin-compounds (neutral fats) are widely distributed. Their compounds with alkalies (soaps) are found in the intestinal canal, and also, to a slight extent, in the blood.

2. Neutral Fats.—The ordinary fats stored up in fat cells, and most of those in the blood and other parts, are neutral fats. Those of most common occurrence in man are *palmitin* and *olein,* and in much smaller amount, *stearin.* Olein is fluid, at the ordinary temperature, while palmitin and stearin require the temperature of the living body to retain them in a liquid state. When treated with an alkali, they take up water, and decompose into glycerin, and their respective fatty acids, which unite with the alkali, and form soaps. They are also decomposed in the same manner by the fat-decomposing ferment of the pancreatic juice. The neutral fats under consideration are constituted by the substitution of the three molecules of the radicles of the respective fatty acids, for the three H atoms of the hydroxyl groups of the glycerin alcohol. Thus:—

Glycerin.	Stearin.	Palmitin.	Olein.
$\left.\begin{array}{r}C_3\ H_5\\ H_3\end{array}\right\}O_3$	$\left.\begin{array}{c}C_3\ H_5\\ \underbrace{(C_{18}\ H_{35}\ O)_3}_{\text{Radicle of Stearic acid.}}\end{array}\right\}O_3$	$\left.\begin{array}{c}C_3\ H_5\\ \underbrace{(C_{16}\ H_{31}\ O)_3}_{\text{Radicle of Palmitic acid.}}\end{array}\right\}O_3$	$\left.\begin{array}{c}C_3\ H_5\\ \underbrace{(C_{18}\ H_{33}\ O)_3}_{\text{Radicle of Oleic acid.}}\end{array}\right\}O_3$

The following graphic formula will serve as a type to show how the production of these compounds results:—

$$\overset{\text{Glycerin.}}{\left.\begin{array}{r}C_3\ H_5\\ H_3\end{array}\right\}O_3} + 3\overset{\text{Palmitic Acid.}}{\left.\begin{array}{l}C_{16}\ H_{31}\ O\\ H\end{array}\right\}O} = \overset{\text{Palmitin.}}{\left.\begin{array}{c}C_3\ H_5\\ (C_{16}\ H_{31}\ O)_3\end{array}\right\}O_3} + 3\overset{\text{Water.}}{\left.\begin{array}{c}H\\ H\end{array}\right\}O}$$

The fats of the body, although derived from the fat in the food, also largely spring from the transformation of the proteid substances. It has been already shown that certain vegetable cells—the bacteria—can bring about the production of fat from proteids during putrefactive fermentation. There is certain evidence, afterwards to be detailed, that the cells of the mammary glands produce fat from proteids, and there is every reason for believing that fats are also derived from carbohydrates.

3. GLYCERIN-PHOSPHORIC ACID, $C_3 H_9 P O_6$, is closely allied to the neutral fats. It is an acid glycerin ether, and may be prepared synthetically from glycerin and orthophosphoric acid. It is obtained from the decomposition of lecithin.

4. ACIDS OF THE LACTIC SERIES.—Lactic and carbonic acids are the members of this series of most physiological interest.

a. Lactic acid, $C_3 H_6 O_3$, is formed from sugar by the lactic acid fermentation. It is found in the alimentary canal, where it results from fermentation of the saccharine elements of the food.

b. Sarcolactic acid, a body isomeric with lactic acid, is produced in muscle during contraction. The mode of its formation is unknown.

c. Carbonic acid, $C H O_3$, is the chief oxidation product of the various organic constituents of the body. It is mostly formed in the tissues, and passes into the lymph and blood, to be excreted by the lungs. It occurs in the form of carbonates, in combination with sodium phosphate, and in a free state.

5. COMPLEX AZOTISED FATS.—1. *Lecithin*, $C_{44} H_{90} N P O_9$, is widely distributed in the body. It is largely present in the brain, nerves, pus, and white blood-corpuscles, ovum, and indeed in protoplasm generally.

2. *Cerebrin*, $C_{17} H_{33} N O_3$?, is a constituent of nerve tissue. The substance described as "protagon," by Liebreich, appears to be a mixture of lecithin and cerebrin (Hoppe-Seyler, *Op.* 21, Heft 4, § 487).

3. *Neurin* or *Cholin*, $C_5 H_{15} N O_2$, is a product of the decomposition of lecithin.

The chemical processes of the organism belong to the three great types of chemical transformation :—1, *Synthesis ;* 2, *Isomeric change ;* 3, *Decomposition.* What may be termed the *minor synthesis* of proximate principles is doubtless a chemical process of common occurrence in the body, *e.g.* the formation of uric acid from xanthin.

$$\underset{\text{Xanthin.}}{2C_5 H_4 N_4 O_2} + \underset{\text{Oxygen.}}{O_2} = \underset{\text{Uric acid.}}{2C_5 H_4 N_4 O_3}$$

A similar example is afforded in the production of hippuric acid from benzoic acid and glycocin. Thus, if benzoic acid be taken into the organism, it combines with glycocin, a derivative of the metabolism of proteids, and the result of the union—hippuric acid—is excreted by the kidneys.

$$\underset{\text{Benzoic acid.}}{C_7 H_6 O_2} + \underset{\text{Glycocin.}}{C_2 H_5 NO_2} = \underset{\text{Hippuric acid.}}{C_9 H_9 NO_3} + \underset{\text{Water.}}{H_2 O}$$

The most notable substance, however, that results from synthetic metabolism in the animal body is hæmoglobin (p. 37). Its composition is more complex than that of the proteids themselves, and it doubtless results from the union of proteids or their allies with iron or with some substance containing it. Yet in this, as in all the syntheses in the body, there is the union of one or more complex organic substances amongst themselves, or with simple substances such as oxygen or water. They are, so to speak, only *minor* syntheses in comparison with the *major* syntheses of complex organic substances out of the elements of CO_2, NH_3, H_2O, and H_2SO_4, occurring in the plant. *Isomeric change* is probably a common occurrence in bodily metabolism; a familiar example is the transformation of starch ($C_6 H_{10} O_5$) into dextrin ($C_6 H_{10} O_5$) by the salivary ferment. A different arrangement of the atoms in the two molecules is probably the cause of their difference in chemical property. But the great chemical change that characterises metabolism in the animal is the *decomposition* of complex organic molecules. The agencies by which this is effected, at the comparatively low temperature of the body, are only very partially known. There are *simple* decompositions; that is, the complex molecule merely breaks up into two or more whose combined molecular weight is equal to that of the substance decomposed; thus, when the molecules of glucose are thrown into commotion by the lactic acid ferment, they simply decompose into those of lactic acid.

$$\underset{\text{Glucose.}}{C_6 H_{12} O_6} = \underset{\text{Lactic acid.}}{2C_3 H_6 O_3}$$

Sometimes a *simple* decomposition consists in the separation of one or more molecules of water (*dehydration*): thus creatin may by heat be split up into creatinin and water:—

$$\underset{\text{Creatin}}{C_4 H_9 N_3 O_2} = \underset{\text{Creatinin.}}{C_4 H_7 N_3O} + H_2O$$

In some cases decomposition is *hydrolytic*, that is, it is preceded or accompanied by the addition of water. This happens when the lactic acid ferment transforms milk-sugar into lactic acid; thus:—

$$C_{12} H_{22} O_{11} + H_2O = 4C_3 H_6 O_3$$

It need scarcely be said, however, that the addition of water is not in all cases followed by decomposition, for the result may be mere *hydration* and not *hydrolysis*.

A change in the relation of the molecules to oxygen is, however, the great feature that broadly marks the decompositions within the organism. *Deoxidation* sometimes occurs; thus, when proteids are fermented by the pancreatic juice, one of the products is indol ($C_{16} H_{14} N_2$), a substance which, unlike the proteids, contains no oxygen. But *oxidation* is the most common event, and is, above all others, the characteristic feature of the metabolic phenomena of the animal body. Hence it is that an incessant stream of oxygen flows through the organism. The following is an example of a decomposition depending on oxidation:

$$\underset{\text{Butyric acid.}}{C_4 H_8 O_2} + \underset{\text{Oxygen.}}{3O_2} = \underset{\text{Acetic acid.}}{C_2 H_4 O_2} + \underset{\text{Carbonic acid.}}{2CO_2} + \underset{\text{Water.}}{2H_2O}$$

Since the time of Lavoisier the idea has generally prevailed that the mere affinity of oxygen for carbon, hydrogen, etc., with the excitement of the organic molecules produced by heat, are the causes of decomposition in the body, as they are in a burning coal. The comparatively low temperature of the body, 38° C. (100° F.) is a serious obstacle to the entertainment of such a hypothesis, which some have endeavoured to surmount by the theory—now, however, proved to be without sufficient foundation—that the oxygen is in the form of ozone.

Ferments and their Effects.

The subject of fermentation grows daily more important in physiology, pathology, and practical medicine. The digestion of the food is almost entirely the work of ferments. They affect the composition of the blood as it passes through the liver. They probably occur widely in the tissues, and either exist in the blood in its normal states, or speedily appear in it under various abnormal conditions. A ferment (*Bacillum anthracis*) appears certainly to be the cause of splenic fever, and other forms of *zymotic* disease are probably due to them. That they are the determining cause of putrefaction—and that antiseptic agents probably act by destroying them—Pasteur (*Op.* 13, vol. lvi. p. 1189) was the first to maintain, (1863), and to point out the importance of applying this principle in practical surgery ; but the scientific instinct of Lister was needed to grasp the significance of the hint, and to give it practical effect.

Ferments are bodies having the power of inducing chemical changes in others without being themselves consumed. The ferments *produced* within the body are albuminoid matters of unknown composition. They are sometimes termed *unorganised* to distinguish them from the *organised ferments*—such as yeast. As the unorganised ferments are all soluble in some medium, the term *soluble* is sometimes employed to distinguish them, but as they are *non-living*, as contrasted with the organised or *living* ferments, they may be thus designated. The non-living ferments of the body being soluble in water may be filtered without loss of power, and salicylic acid—which is fatal to living ferments—does not prevent their action (Kühne). Non-living ferments are incapable of self-multiplication. Living ferments grow and multiply at the expense of the matters in which they occur, and unless they are suitably fed, they die and become useless.

Non-living or Soluble Ferments.

All the ferments capable of being isolated from the tissues and fluids of the body are *hydrolytic;* that is, they all cause water to be taken up by the substance in which they induce decomposition. Those as yet known may be classified in three groups.

1. *Amylolytic* or *sugar-forming ferments,* formed in the salivary glands, pancreas, liver, and intestinal glands, and present in some other organs. Most of these convert starch and its isomeric ally glycogen, into grape-sugar. The intestinal ferment converts cane-sugar into grape-sugar. These ferments act like dilute mineral acids at a boiling temperature.

2. *A fat-decomposing ferment* formed by the pancreas. It causes neutral fats to take up water, and to split into glycerine and fatty acids at the temperature of the body (38° C.) This ferment produces the same effect as a caustic alkali at a higher temperature than is necessary for the action of the ferment.

3. *Proteolytic ferments* formed by the gastric glands and pancreas transform soluble or coagulated proteids into peptones and other products. The physiology of these ferments will be discussed in detail under Digestion.

Living or Organised Ferments.

To what extent—if indeed at all—the metabolic phenomena occurring in the tissues are to be regarded as of a fermentative nature is unknown. Therefore, for the present, it must be simply stated, that the only living ferments that appear to exist in the body in its normal state are certain fungi found in the alimentary canal. There they appear to give rise to putrefaction of proteid particles—in the sordes around the teeth—and probably also in the lower part of the intestine; and to lactic and butyric fermentations in the stomach. In abnormal states they may find their way into the urinary passages, and induce decomposition of the urine; and they may also enter the blood and other parts, and there become the cause of deadly disease.

YEAST AS A FERMENT.—As yeast is the type of an organised or living ferment, some facts with regard to its action may not be inappropriately stated here. It transforms cane-sugar into grape-sugar, and induces alcoholic fermentation in the latter. About 98 per cent of the sugar is split up into alcohol, carbonic acid, and small quantities of glycerine and succinic acid; while nearly two per cent of the sugar disappears; being probably, as Pasteur suggests, appropriated by the protoplasm of the torula.

Yeast cannot induce alcoholic fermentation *unless it be living.* A boiling temperature, ether, chloroform, carbolic and salicylic acids, creosote, etc., all destroy its vitality, and prevent alcoholic fermentation. Further, unless yeast be supplied with the food necessary for the life of its protoplasm (p. 20)—*e.g.* if it be sown in *distilled* water and sugar—it soon dies, and its power as an alcoholic ferment ceases. It was maintained by Liebig that the fermentative power of yeast is due to a catalytic effect of its azotised matter while undergoing oxidation—he being entirely opposed to the doctrine that the *life* of the yeast is concerned in the result. But when the yeast, sown in distilled water, dies and decomposes, the proteids of its protoplasm are precisely in that condition which, according to Liebig, is favourable to its activity as a ferment. Therefore, however much remains doubtful, this is certain, that yeast *acts as an alcoholic ferment only when it lives.* No one has succeeded in separating an alcoholic ferment from the torulæ, and the only conclusion as yet warrantable is that the living torula is itself the ferment. With regard to the manner of its action we know nothing definite, and have no better theory than that long ago suggested by Stahl,—that the living yeast, being in a state of inward commotion, communicates to the sugar movements that induce it to take up water, and resolve itself into new compounds.

But yeast also produces a non-living *soluble* ferment separable from the torulæ *after they have been killed by ether* (Hoppe-Seyler, *Op.* 42, p. 522), which transforms cane-sugar into grape-sugar, although it cannot carry the change further. The distinction between the *living* alcoholic ferment and the *non-living* glucose-forming ferment in connection with yeast is obviously of great interest, and important in its bearing on the whole question of organised ferments. *By killing the yeast all fermentative power is not abolished, but merely a certain fermentative power dependent on its living state.*

BACTERIA AND THEIR EFFECTS.—Bacteria are elementary organisms having the characters of fungi. They appear to be minute non-nucleated particles of protoplasm enclosed in a cellulose envelope. They live readily in fluids containing proteid matter in solution, but, like fungi, they can also thrive in Pasteur's fluid (p. 20). Like yeast, they require oxygen, which they may obtain from the air dissolved in the fluid, or from some decomposable organic substance which contains it.

Our knowledge of bacteria is as yet so imperfect, that classifications hitherto proposed can only be regarded as temporary. Cohn (*Op.* 35, i. p. 146) proposes to divide them into four groups—1. *Globular* bacteria, represented by *Micrococcus* (Fig. 10). 2. Rod-like bacteria, *Bacterium termo* (Fig. 11). 3. *Thread-like* bacteria, including *Bacillum* and *Vibrio.* 4. *Spiral* bacteria, including *Spirillum* and *Spirochæte.* The researches of Lister (*Op.* 8, vol. xiii. p. 381) have, however, very clearly proved the inadequacy of any classification—such as Cohn's—based exclusively on morphological features, for the rod-like bacterium (*Bacterium lactis*) that occasions the lactic acid fermentation, assumed thread-like and toruloid forms when sown in urine, rod-like forms when transferred from the urine to Pasteur's fluid, thread-like and rod-like forms when re-transferred from the Pasteur's fluid to urine, and rod-like and thread-like forms after it was re-transferred to boiled milk. Yet, notwithstanding the various fluids in which it had been sown, and which had effected notable changes in its morphological characters, its physiological property of inducing lactic acid fermentation was retained. Thus, it seems evident that a classification of bacteria on physiological, instead of morphological grounds, will have to be adopted. This is also very strikingly illustrated by the fact that the bacterium which occasions butyric fermentation (*Bacillum subtilis*) and the bacterium which induces splenic fever (*Bacillum anthracis*) are *identical in morphological characters and in life-history;* yet when *B. subtilis* is injected under the skin of an animal no evil effects ensue, but when *B. anthracis* is injected, "splenic fever," and it may be death, are the result.

This *difference of physiological effect with identity of morphological character* is a cardinal point in the considerations that cluster around bacteria.

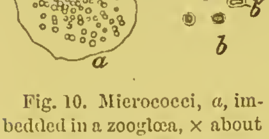


Fig. 10. Micrococci, *a*, imbedded in a zooglœa, × about 400; *b*, free and more highly magnified; *b′ b′*, undergoing division.

Micrococcus.—If a piece of unboiled meat be triturated with cold water, the fluid filtered, and placed in an ordinary vessel, and kept at summer heat, it becomes in a day or two somewhat turbid, and a scum or pellicle appears on the surface. The pellicle consists of a multitude of minute globular bacteria—*micrococci*—imbedded in a clear jelly termed *zooglœa* (Fig. 10, *a*). The zooglœa is analogous to that produced around the familiar alga—*palmella*, but whether it is secreted by the micrococci or produced from substances in the surrounding fluid by a sort of fermentative influence is unknown. Micrococci are exceedingly minute, being only about 1 μ ($\frac{1}{25000}$ inch) in diam. They are comparable to torulæ in so far as they are minute particles of protoplasm, in what appears to be an envelope of cellulose. Unlike torulæ, however, they proliferate by fission (*b′ b″*). In their jelly, micrococci exhibit no locomotion, but when free, and not clinging to any fixed objects, they exhibit an irregular dancing movement, which, so far as we know at present, seems to be *Brownian motion;* an irregular vibratory movement common to all fine particles floating in a fluid. It is purely physical, and probably results from thermal changes in the fluid.

Bacterium termo may also be found in great numbers with micrococci in the putrefying juice of meat as well as in other putrefying fluids. It sometimes consists of one, mostly of two, and rarely of three or more segments. Its breadth is usually about 1 μ, and the length of one segment usually 1·5 μ (Cohn). But—as in *Bacterium lactis*—the length of the segment probably varies according to the conditions under which the fungus grows. When enveloped in a zooglœa (Fig. 11, *a*), *B. termo* is motionless; when perfectly free, it moves. It exhibits two sorts of movements:—1, a vital movement; and 2, Brownian movement. The vital motion is due to the contractions of a pair of cilia or flagella—one at each end of the minute cell (*c″*). The flagella lash like the tail of a fish, and impel the individual in a *definite direction.* They are analogous to the flagella seen on the familiar *protococcus,* and as in that case, so here, they are doubtless prolongations of the protoplasm through the cellulose envelope.

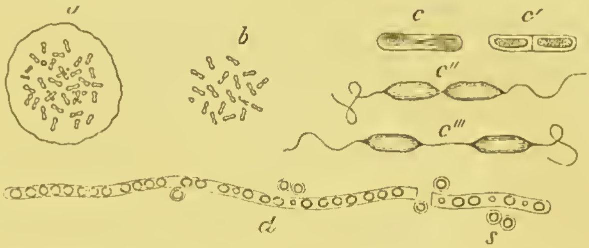


Fig. 11. *Bacterium termo, a,* forming a zooglœa; *b,* free, × 600 *c c′,* dividing; *c″,* with flagella; *c‴,* division nearly complete, with growing flagella forming a connecting link (after Dallinger): *d,* Bacterium elongated to form a gonidium- or "spore"-containing filament; *s,* germs or "spores." (After Ewart.) × 4000.

Sometimes the flagella cease to lash, and the movement of the bacterium in a definite direction stops; and it can at any time be brought to an end, *e.g.,* by a boiling temperature or by alcohol. But although the vital movement ceases, Brownian motion, always present, but obscured by the vital movement, continues, so that, when the free bacterium becomes "quiescent," it is quiescence only as regards the vital motion in a definite direction. The living bacteria on becoming quiescent may secrete a zooglœa, and thus produce a colony (*a*).

The flagella of *Bacterium termo* were recently discovered by Dallinger and Drysdale (*Op.* 9, vol. xiv. p. 105), and notwithstanding their extreme tenuity, have been measured by the former, who finds them to be $\frac{1}{204700}$ inch in breadth, a size almost inappreciable. Recently Koch (*Op.* 35, year 1877) has actually succeeded in taking a microphotograph of the flagella and bacterium.

Bacterium termo commonly multiplies by fission. After magenta-staining, the protoplast may be seen in the act of division (*c*). In others the division appears to be complete, but in reality a minute protoplasmic thread unites the two segments. It afterwards elongates and forms a flexible link (*c‴*) that remains for a variable period, but finally snaps and forms two flagella. Another mode of reproduction, discovered by Koch (*Op.* 35, vol. ii. p. 3) in the case of *Bacillum anthracis,* and recently pointed out by Ewart in this particular instance (*Op.* 4, vol. xxvii. p. 474), consists in the formation of germs or gonidia; the bacterium elongates (*d*); its protoplasm repeatedly divides, and eventually forms small, bright, refracting particles, each with a thin envelope. The parent envelope gives way and they escape. That these are really germs was proved by Koch (*Op. cit.*) who observed them, in the case of *Bacillum anthracis,* sprouting and elongating into filaments.

As regards the relation of *Micrococcus* to *Bacterium termo*, further investigation is needed. It is maintained by Cienkowski (*Op.* 43) that micrococci arise by repeated subdivision of bacteria, and it has been generally supposed that micrococci elongate and produce bacteria (Cohn, *Op.* 35, vol. i. p. 149); but doubt has been thrown on this by Ewart, who in his experiments succeeded in getting a cultivation where micrococci without any rod-like bacteria were present. The preparation was made by inoculating a drop of fresh aqueous humour (an albuminous fluid) from the eye of an ox by a minimal quantity of pus taken from a newly-opened abscess on the point of a calcined needle (*Op.* 4, vol. xxvii. p. 476), the fluids being rapidly placed on a calcined glass slip and under a calcined cover-glass, and sealed.[1] No elongation of micrococci into the rod-like bacteria could be detected, although watched for many days.

Bacterium termo is believed by many to be probably the great cause, though possibly not the only one, of putrefactive fermentation of albuminous substances. The effect of micrococcus is not so clear, but it is also very commonly present where putrefactive change is taking place; this subject will, however, be discussed later.

Bacillum.—The *Bacillum subtilis* of butyric fermentation, and the *Bacillum anthracis* (Fig. 12), the ferment of splenic fever, are morphologically identical, and have a life-history so similar to that of *Bacterium termo*, already described, that a special account need not be given.[2] The segments of *Bacillum* are usually longer than those of *Bacterium termo*, but under special circumstances those of the latter sometimes attain to greater length. The totally different physiological effects of *B. subtilis* and *B. anthracis* have already been mentioned.

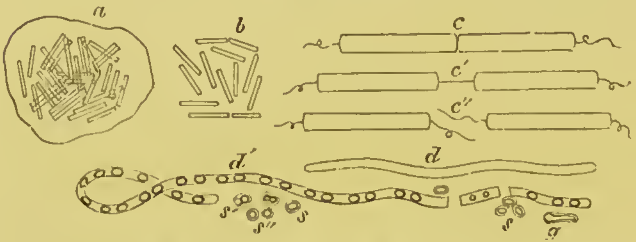


Fig. 12. *Bacillum anthracis*, *a*, in a zooglœa; *b*, free; *c c′*, dividing; *c′* divided; *d*, elongating to form a gonidium- or "spore"-containing filament *d′*; *s*, spores; *s′ s″*, gonidia dividing; *g*, gonidium sprouting to form a filament. Highly magnified. (Ewart.)

Effects of Reagents on Bacteria.—*a. Heat.*—That fully formed bacteria are killed by ebullition is what might be expected, indeed, a much lower temperature than 100° C. (212° F.) is sufficient: thus, while *Bacterium termo* multiplies rapidly between 30° and 35° C., it is killed by a fourteen hours' exposure to 40° C., or a three hours' exposure to 45° C. (Eidam, *Op.* 35, vol. i. p. 223). The *germs* of bacteria, however, are not so easily killed. In the *dry state* they may be heated to 110° C. (230° F.) without losing their vitality (compare effect of heat on dried albumin, p. 35), but they are destroyed by a temperature of 120° C. (248° F.) Sanderson and Ewart (*Op.* 4, vol. xxviii. p. 477). In a *moist condition* the germs are destroyed at a lower temperature, but as Tyndall (*Op.* 3, vol. clxvii. p. 149) has conclusively shown, it is an error to suppose that ebullition for *a few minutes* is in all cases sufficient for their destruction. Thus he found from a large number of experiments, that the bacterial germs in *old* hay, when boiled in an infusion of turnip, are not with certainty sterilised by ebullition, unless it be continued for *four hours* (*lib. cit.* p. 177). In an infusion of cucumber, the vital resistance of the germs was found to be quite as great. Ignorance of this fact has been the cause of much trouble to those desirous of proving the *groundless supposition* that bacterial and other *small* things may arise *de novo* in turnip infusion and similar fluids. The probable explanation of this remarkable fact—that *dried* bacterial germs are, as above stated, not killed by temperature under 120° C. (248° F.)—is, that the envelope of the germ becomes by desiccation extremely impervious to moisture, and requires to be exposed to even *boiling* water for several hours before it is penetrated and the protoplasm destroyed

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[1] These precautions are needed to destroy the germs of other fungi.

[2] The term *Bacillum* might well be abandoned and *Bacterium* substituted; for the former only introduces needless confusion, and in point of etymology is indefensible, for while *βάκτρον* means a *staff* or rod, *bacillum* is the diminutive of *baculum* and means a *little staff.* Yet *Bacillum* is applied to a body longer than the ordinary *Bacterium termo.*

Pasteur in 1862 (*Op.* 44, vol. lxiv.) observed the singular fact, that while *acid* fluids are sterilised by a temperature of 100° C., a few degrees more are needed to sterilise alkaline fluids ; *e.g.* alkaline urine.

b. Chemical Reagents.—Bacteria are killed by carbolic acid, salicylic acid, alcohol, and various other antiseptic agents. Paul Bert (*Op.* 13, vol. lxxx. p. 1579), has recently shown that when flesh, moist bread, fruits, wines, etc., are exposed to *pure* oxygen, under pressures varying from ten to twenty-seven atmospheres, putrefaction is entirely prevented, and it required a long subsequent exposure to common air to bring it about. The effect cannot be mechanical, for such pressures with *ordinary air* instead of with pure oxygen entirely fail to sterilise the putrefactive germs.

BACTERIA AS FERMENTS.—That a bacterium, named by Lister the *Bacterium lactis*, is the cause of lactic acid fermentation was long ago surmised by Pasteur, and has been completely proved by Lister (*Op.* 8, vol. xviii. p. 177). It is just as certainly the cause of lactic fermentation, as yeast is of alcoholic fermentation. The remarkable morphological changes which the *Bacterium lactis* undergoes when sown in different fluids, with retention, however, of its lactic fermentative power, have been already alluded to.

That the *Bacillum subtilis* is the cause of the butyric fermentation is highly probable, while it seems certain that the *Bacillum anthracis* is the cause of splenic fever,—which is therefore probably of the nature of a fermentation. Many are equally convinced that putrefaction is also due to ferments, and that the particular ferment is notably the *Bacterium termo.* Wherever putrefaction is taking place, bacteria are found growing and multiplying, and the question arises,—Are they themselves the destructive agents that occasion putrefactive change, or do they merely revel amidst the chaos of its results, like sea-fowl in the wake of a vessel? There are some who—following the teaching of Liebig, that putrefaction is merely due to oxidation—incline to the latter idea. But it becomes untenable when narrowly examined.

1. A watery solution of peptones (p. 36) is a fluid rich in proteid matter; apt to putrefy, and having the advantage over an ordinary albuminous fluid of not coagulating on heating. Such a solution made of a specific gravity about 1005 putrefies when placed in any ordinary vessel, and kept at 30-35° C. If the unboiled fluid be placed in a flask that has not been exposed to a high temperature—it matters not whether its mouth be open, or closed with a cork, or glass stopper, or plug of cotton-

wool—it in time swarms with bacteria. 2. If say half a dozen glass flasks be half filled with the solution of peptones, their mouths firmly plugged with cotton-wool, and all placed in a water bath, boiled for an hour or so, and then set aside and kept at the moderate temperature of 30-35° C., putrefaction scarcely ever ensues, and yet there is oxygen in the air of the flask ready to oxidise the proteid material, if that were enough to occasion putrefaction. But as soon as the merest trace of bacterial scum is introduced into the fluid in the flask, and the cotton-wool plug replaced, putrefaction begins, and though it were a flask capable of holding a large quantity of peptone fluid, it would be found that after inoculation with a minute particle of bacterial scum, the merest trace of the putrefying fluid could in turn excite putrefaction in another; evidently because the putrefactive ferment is capable of self-multiplication. But if the bacterial fluid be thoroughly boiled, it no longer serves to induce putrefaction in another. On Liebig's theory this seems inexplicable, for why should the temperature of boiling water destroy the cause of fermentation in a NON-COAGULABLE fluid if *that cause be not living?* There is but one feasible explanation—viz. *that putrefaction is due to a ferment, and that ferment is living bacteria.* To inoculate such fluids with putrefactive ferment, bacterial scum is not essential, a drop of ordinary unboiled water, or the contact of any solid body not exposed to a sufficient heat, or to other antiseptic agents such as carbolic acid, may suffice to introduce the putrefactive ferment, for bacterial germs contaminate the outer surfaces of all solids, and exist in air as well as in water. Some indeed have stated that bacterial germs are not conveyed through the air, but only by water and solids; it need not be doubted, however, that this is an error.

We are indebted to Lister (*Op.* 8, xviii. p. 179) for proof of the fact that putrefactive germs do not exist in the blood, in its normal condition at all events. Thus, if blood be run from the vein of an animal through a calcined glass tube, into a glass flask that has been heated to 300° F., and allowed to cool in a chamber whose air has been purified by the fine spray of carbolic acid, the flask may be kept simply covered with an inverted watch-glass and under a bell-jar without putrefaction; yet, under these conditions, if the blood be inoculated with bacteria, it putrefies rapidly. Lister also showed that the same holds true of milk with regard to the *Bacterium lactis*, it is not present in the milk when secreted, but appears in it only after external contamination. Chiene and Ewart (*Op.* 1, vol. xii. p. 448) have made experiments on this point, and have supplemented Lister's observations by demonstrating that in living healthy rabbits neither bacteria nor their germs exist in the liver, spleen, kidneys, pancreas, lymphatic glands, and urinary bladder, although they exist in great numbers in the stomach.

There is therefore a sound scientific basis for that system of surgery devised by Lister, which seeks to prevent putrescence of the exposed fluids and internal solids of the body by guarding them from the entrance of the germs of putrefactive ferments. (The effects of putrefactive ferments on proteids have been stated at p. 39.)

In addition to the works referred to in the text, consult those mentioned by Ray Lankester in *Op.* 8, vol. xviii. p. 455.

SECTION II.

PHYSIOLOGY OF THE TISSUES.

ENUMERATION OF THE TISSUES.

THE term *tissue* has by some been confined to coherent groups of similar morphological units, such as epithelial and cartilaginous tissues. The blood-corpuscles being detached units floating in a fluid, do not fall within this definition. It is therefore more convenient to give a less restricted meaning to the term, and to apply it generally to all the elementary organised constituents of the body. The elementary tissues may be grouped as follows :—

- Blood and lymph corpuscles.
- Epithelial tissue.
- Connective tissues
    - Cartilaginous tissues.
    - Mucous tissue.
    - Retiform tissue.
    - Ordinary connective tissue.
    - Osseous tissue.
- Adipose tissue.
- Dental tissues.
- Muscular tissue.
- Nerve tissues.

The bodily *organs* consist of assemblages of two or more elementary tissues.

CHAPTER VI.

BLOOD-CORPUSCLES.

THE blood consists of corpuscles in a fluid—the plasma, or *liquor sanguinis.* The corpuscles are chiefly of two sorts, coloured and colourless ; and in addition to these there are some minute particles, the so-called "granules of the blood."

The colourless corpuscles are found in the blood of all animals. In the invertebrata and in the lowest vertebrate (*Amphioxus lanceolatus*) the corpuscles are *all* colourless. In all other vertebrates two kinds of corpuscles occur, and the *coloured* are more numerous than the *colourless* corpuscles.

The colourless having a simpler structure than the coloured corpuscle, and, preceding it in the order of development, will be studied first.

WHITE BLOOD-CORPUSCLES.

In all animals the colourless blood-corpuscles are nucleated masses of amœboid protoplasm.

White Corpuscles of Newt's Blood.—Amphibians having larger blood-corpuscles than other animals, their blood is particularly suited for microscopical study, and the blood of the newt is preferable to that of the frog, on account of the larger size of its corpuscles, and also because of other points of difference. If a drop of blood be drawn from the tail of the newt, placed on a glass slip, and covered, before it coagulates, with a thin glass, and then magnified about 300 diam., the corpuscles may be readily seen, but a magnifying power of 1000 diam. is more advantageous.

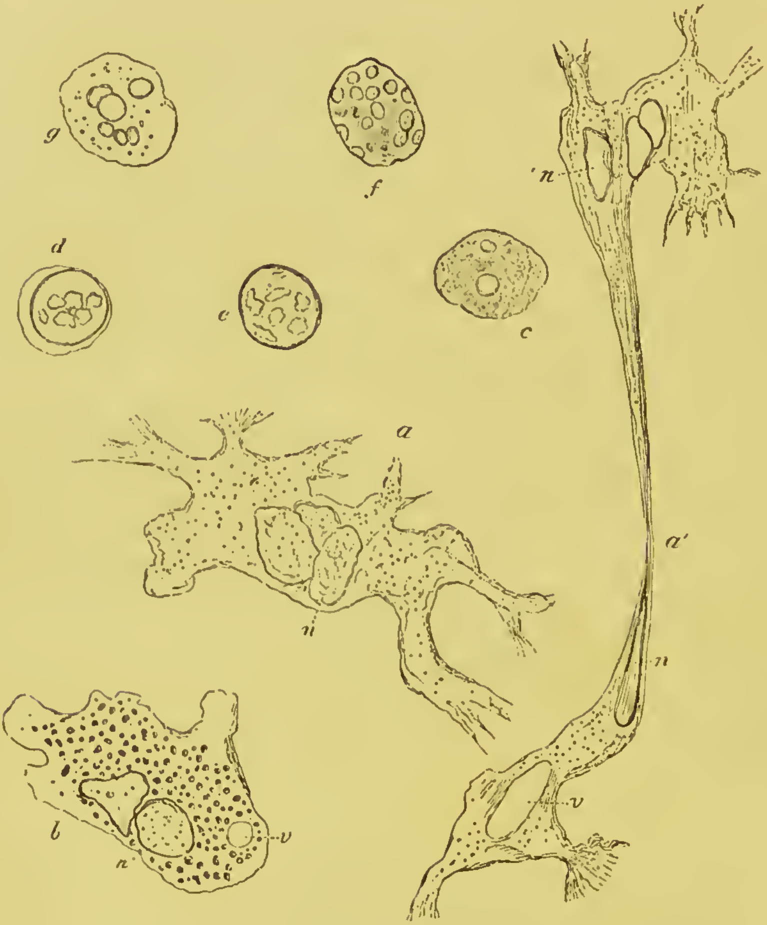

Fig. 13. Colourless corpuscles of newt's blood. *a*, Large finely-granular corpuscle. *a'*, The same corpuscle half an hour later. *b*, Coarsely-granular corpuscle; *n*, nuclei; *v*, vacuole; c, *d*, *g*, small white corpuscles. All the above corpuscles are contractile. *e*, *f*, Motionless corpuscles, probably old nuclei of coloured corpuscles. X 450.

In the newt's blood the white corpuscles may be divided into three varieties: 1. *The large finely-granular corpuscle* (Fig. 13, *a*, *a′*). 2. *The coarsely-granular corpuscle* (*b*). 3. *The small white corpuscles* (*c*, *d*. *g*).

1. *The large finely-granular corpuscle* is the most common variety. It is about 62 μ ($\frac{1}{400}$ inch) in diam., and is a mass of finely-granular protoplasm, with two or three nuclei, but without any evident envelope (periplast). The corpuscle is *inelastic,* and decidedly *viscous.* In consequence of its viscosity it tends to cling to the lining membrane of the blood-vessels, as may be witnessed in the tadpole's tail or frog's web.

The corpuscle is contractile, and exhibits amœboid movements, by which it can migrate from place to place. It can even emigrate from the blood through the walls of the capillaries and smaller veins into the surrounding tissues. This emigration (*diapedesis*), first demonstrated by Augustus Waller (*Op.* 36, year 1846), and re-discovered by Cohnheim (*Op.* 19, vol. xl., year 1867), may be observed at any time in the tadpole's tail (Fig. 14), but it occurs more especially during the process of inflammation. The emigration is very tardy, and that of a single corpuscle may occupy from one to three hours.

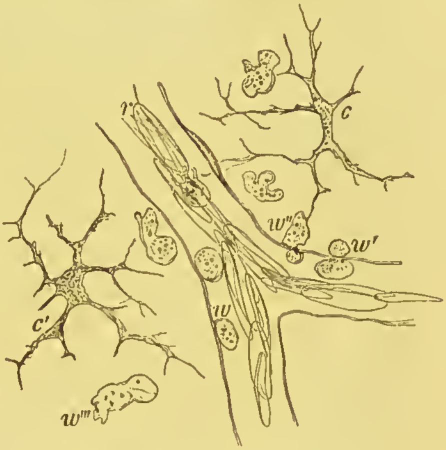

Fig. 14. Diapedesis of white blood-corpuscles through the wall of a capillary in the tail of a tadpole. *w*, White corpuscle clinging to the wall of the vessel; *w′ w″*, white corpuscles emigrating; *w‴*, emigrated white corpuscle; *c c′*, connective tissue corpuscles; *r*, coloured blood corpuscles. × 300.

The pseudopodia of the corpuscle may fuse together at their apices, and the facility with which they do this seems to preclude the idea of the existence of an envelope. Sometimes they enclose a drop of fluid, and thus a vacuole (*v*) is formed in the protoplasm. Vacuoles, however, usually arise—not in this manner—but by some internal centrifugal movement of the protoplasm, whereby it leaves a space in its midst filled with fluid. Sometimes the corpuscle becomes elongated, its extremities move in opposite directions, while the intervening portion becomes more and more attenuated (*a′*, Fig. 13) and may finally give way. Occasionally the extremity of a protoplasmic process becomes detached in this manner.

2. *The coarsely-granular corpuscle* (*b*, Fig. 13) is not nearly so numerous as the first variety. It is a nucleated mass of coarsely-granular protoplasm. It usually exhibits active amœboid movement. The protoplasm streams out into pseudopodia, that are usually at first perfectly clear and homogeneous, until the granules suddenly start off and run into them. When there is a general excitement of the mass one may often see a set of granules moving in one direction, while a neighbouring set moves the opposite way:—as in the protoplasm of the Tradescantia cell (Fig. 6).

3. *The small white corpuscles* present various appearances. In one sort (*c*) there are one or two nuclei in a considerable mass of finely-granular protoplasm. In another (*g*) the nuclei are more numerous, and the protoplasm more transparent. In a third (*d*) there is a large nucleus surrounded by a relatively small quantity of protoplasm. All of them exhibit amœboid motion.

There are other corpuscles (*e*, *f*) which, though colourless, are of a different nature from the white corpuscles proper. They refract light strongly, and have no amœboid movements. They are probably the free nuclei of broken down coloured corpuscles[1] (compare *d*, Fig. 18).

ENTANGLEMENT OF SOLID PARTICLES.—Like the amœba, the protoplasm of the white corpuscles can entangle and envelope solid particles. Thus, if carmine, vermilion, indigo, or aniline-blue be reduced to a state of very fine division, mixed with serum or dilute albumin, and added to a drop of newt's blood—gently heated (30° C.) to hasten amœboid movement—the coloured particles are, as it were, eaten by the corpuscles. The importance of this observation—first made by Schultze (*Op.* 18, i. p. 1)—has been shown by Cohnheim, who injected finely divided aniline-blue into a subcutaneous lymph sac of the frog. The lymph corpuscles (young white blood-corpuscles) enveloped the pigment granules, and entered the circulation. After some days, inflammation of the cornea was artificially induced. Pus-corpuscles appear in the cornea, and in many other parts when inflamed. Virchow taught that all the pus corpuscles in this case arise from proliferation of the connective tissue corpuscles of the cornea. Probably some of them do arise in this way, but Cohnheim proved that, at all events, many of them are white blood-corpuscles that have emigrated from the vessels at the margin of the cornea; for he found that when he irritated the corneæ of frogs having their blood-corpuscles artificially pigmented, many of the pus cells in the cornea contained blue pigment granules. The structural characters of pus cells are identical with those of white blood-corpuscles.

EFFECTS OF REAGENTS.—*Magenta*, *carmine*, and some other dyes brilliantly stain the nuclei, and to a less extent the surrounding protoplasm.

Dilute acetic acid, or dilute solutions of *caustic alkali*, arrest the amœboid motion, by paralysing the protoplasm, which they render extremely transparent, and thus reveal the nuclei, on which, however, they appear to havo little effect (Fig. 20, *b*).

Water, when added in sufficient quantity, paralyses the protoplasm, which swells up from endosmose.

Electricity and *heat* produce effects similar to those already described in the case of the amœba (p. 24).

WHITE CORPUSCLES OF HUMAN BLOOD.—When a drop of human blood is placed under the microscope, it is at first somewhat difficult to detect the white corpuscles, owing to their relatively small number. Ere long, however, the coloured corpuscles run into rouleaux (Fig. 15, *c*), leaving the white corpuscles (*w*, *w'*) more or less isolated in the meshwork. The ordinary white corpuscle of human blood (Fig. 16, *c*, *d*) resembles the common white corpuscle of newt's blood in every respect save size. It is a mass of nucleated amœboid protoplasm, without any apparent envelope. The nuclei vary from one to five; usually there are three. The corpuscles vary from 8 μ to 16 μ ($\frac{1}{3200}$ to $\frac{1}{1600}$ inch) in diameter, that is, from about the same size to twice the size of the coloured corpuscle.

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[1] When a drop of newt's blood has been kept for some time between two slips of glass, the coloured corpuscles become decidedly altered: amongst other things, their nuclei become extravasated. The forms *e* and *f* in Fig. 13 may, however, be seen in perfectly fresh blood.

Sometimes one may find in a drop of human blood a coarsely-granular corpuscle resembling that of the newt's blood (Fig. 13, *b*), and in every drop of blood one may with a very high power (1000 diam.) see here and there, as Beale was the first to show, extremely minute non-nucleated particles of protoplasm, some of which are probably detached from the pseudopodia of the larger corpuscles.

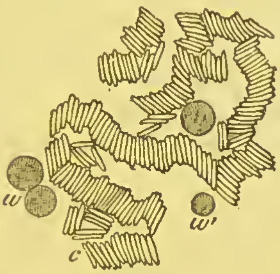

Fig 15. Human blood. *c*, Coloured corpuscles in rouleaux; *w*, *w′*, white corpuscles. × 300.

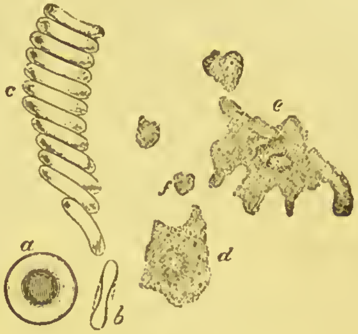

Fig. 16. Human blood corpuscles. Coloured corpuscle lying (*a*) on its broad surface (*b*) on edge; *c*, rouleaux of coloured corpuscles; white corpuscles nucleated (*d*, *e*); without nuclei (*f*). × 1000.

As regards amœboid movements and the effects of re-agents, the statements already made regarding the newt's corpuscles are applicable here, with this difference, however, that as the human corpuscles are normally at a temperature of 38° C. (100° F.), they require to be kept at that temperature to show their amœboid movements perfectly.

The term *leucocyte* is applied by some to lymph-cells and white blood-cells, the wandering cells of connective tissue, and pus-cells. All these corpuscles have a similar structure, and most of them a similar origin.

Chemical Composition.—Owing to the impossibility of isolating the white corpuscles in numbers sufficient for analysis, their chemical composition cannot be directly ascertained. Doubtless they have a composition similar to that of undifferentiated protoplasm generally. As pus-corpuscles, however, are optically identical with, and in many cases are emigrated white blood-corpuscles (p. 54), their composition is probably similar to that of the blood-corpuscles.

Pus-corpuscles contain several proteids—one closely allied to myosin, and another to alkali-albumin. There is also a relatively large proportion of a carbohydrate—glycogen, and an azotised fat—lecithin. The chief salt is potassium-phosphate. The nuclei contain nuclein (p. 37).—Miescher, *Op.* 21, *Heft* 4, p. 441.

COLOURED BLOOD-CORPUSCLES.

Colour and Shape.—In all animals the coloured corpuscles are *red* when seen in mass, but *pale yellow* when viewed singly. Their pigment is hæmoglobin (p. 37). They have no amœboid or other contractile motion, and although very extensible they are perfectly elastic, and therefore have shapes that are definite, unless when distorted by pressure. Possessing a smooth and non-viscous surface, they readily glide past each other within the blood-vessels. They present two types as regards *shape*, and two as regards *structure.* Thus, with regard to *shape,* they are—1. *Circular biconcave discs* in all mammals excepting the camel tribe, and in some cyclostomatous fishes; 2. They are *oval* and *biconvex* in all other vertebrates, viz. in fishes, amphibians, reptiles, birds, and in the camels. In point of *structure*—1. They are non-nucleated in all mammals; 2. they are nucleated in all other vertebrates.

SIZE.—As regards size, they vary greatly in different animals, being largest in amphibians, and smallest in mammals. A conception of their relative sizes throughout the vertebrata generally may be obtained from Fig. 17.

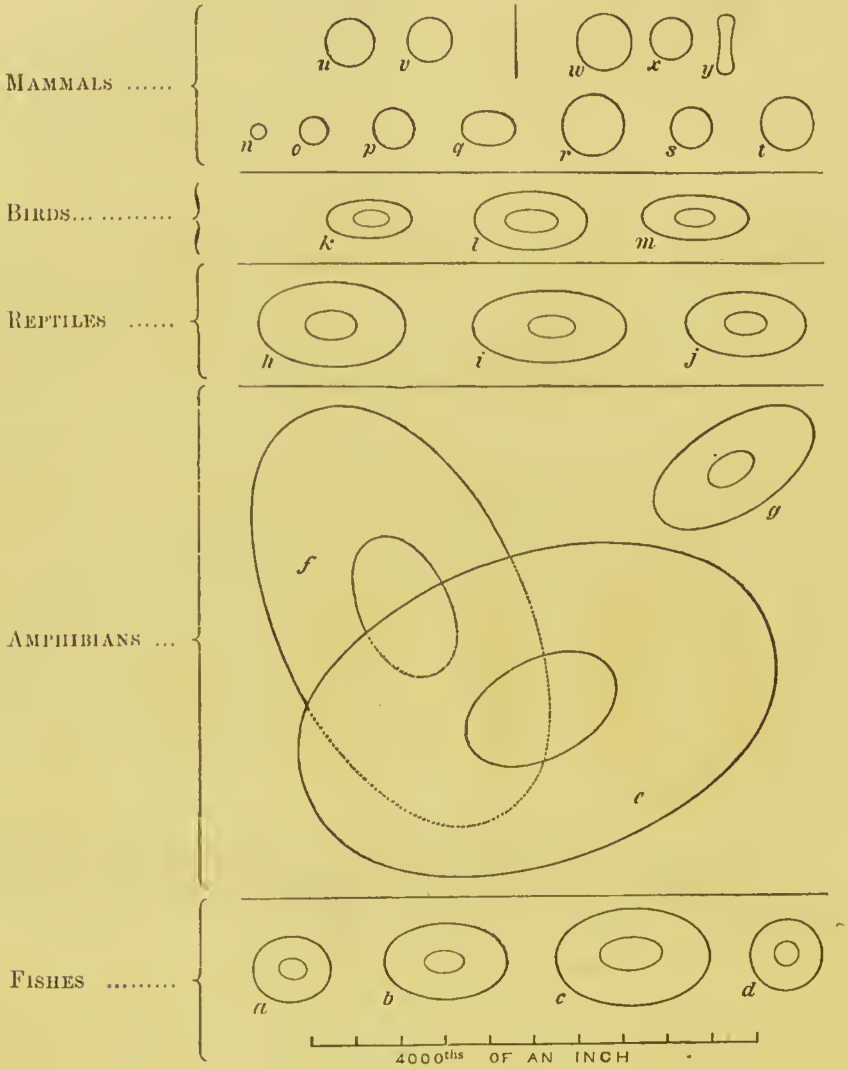

Fig. 17.

a = Tench.
b = Salmon.
c = Dog-fish.
d = Ammocœtes.
e = Amphiuma.
f = Proteus.
g = Toad.
h = Snake.
i = Slow-worm.
j = Lizard.
k = Pigeon.
l = Ostrich.
m = Owl.
n = Musk-deer.
o = Deer.
p = Ox.
q = Camel.
r = Elephant.
s = Horse.
t = Dog.
u = Ateles ater. } Quadrumana.
v = Chimpanzee. }
w = } Man.
x = }
y = „ seen on edge.
(After *Gulliver.*)

The relative size of the coloured corpuscles being important from a medico-legal point of view, the following measurements in fractions of an inch are given by Gulliver (*Op.* 37, xli. p. 474).

	Diameter.
Man	$\frac{1}{3200}$
Chimpanzee	$\frac{1}{3412}$
Cat	$\frac{1}{4404}$
Dog	$\frac{1}{3542}$
Horse	$\frac{1}{4600}$
Elephant	$\frac{1}{2476}$
Pig	$\frac{1}{4230}$
Musk-deer	$\frac{1}{6300}$
Sheep	$\frac{1}{5300}$
Ox	$\frac{1}{4267}$
Rat	$\frac{1}{3754}$
Mouse	$\frac{1}{3814}$
Rabbit	$\frac{1}{3607}$

	Long Diameter.	Short Diameter.
Camel	$\frac{1}{3123}$	$\frac{1}{5876}$
Ostrich	$\frac{1}{1649}$	$\frac{1}{3000}$
Duck	$\frac{1}{1937}$	$\frac{1}{3424}$
Fowl	$\frac{1}{2102}$	$\frac{1}{3466}$
Green Lizard	$\frac{1}{1555}$	$\frac{1}{2743}$
Snake	$\frac{1}{1274}$	$\frac{1}{1800}$
Frog	$\frac{1}{1108}$	$\frac{1}{1821}$
Proteus	$\frac{1}{400}$	$\frac{1}{727}$
Amphiuma	$\frac{1}{363}$	$\frac{1}{615}$
Cod	$\frac{1}{2133}$	$\frac{1}{3555}$
Salmon	$\frac{1}{1524}$	$\frac{1}{2460}$
Herring	$\frac{1}{2000}$	$\frac{1}{3555}$

COLOURED BLOOD-CORPUSCLES OF THE NEWT.—The coloured blood-corpuscle of the newt is a convenient example of the nucleated red corpuscle. It is oval (Fig. 18, *a*), and when viewed in profile flattened and biconvex (*b*). It is transparent and pale yellow. Immediately after withdrawal from the circulation it appears to be homogeneous, but ere long a nucleus becomes evident as a light spot in the centre (*c*). In perfectly fresh blood one may sometimes find a corpuscle of the same size and shape as the normal coloured corpuscle, but devoid of colour, and with a very evident vacuolated nucleus (*d*). In others vacuoles may be sometimes seen in the perinuclear substance. Such appearances probably indicate regressive metamorphosis.

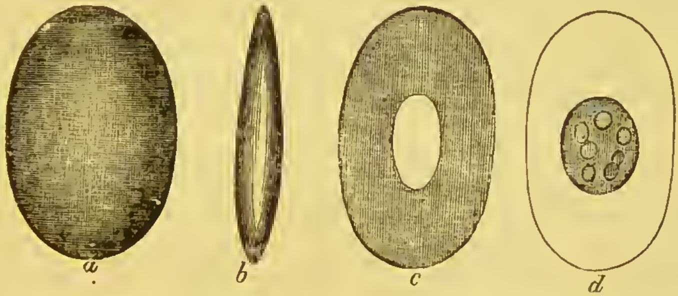

Fig. 18. Coloured blood-corpuscles of newt. *a*, Corpuscle on its broad side; *b*, on edge; *c*, altered by exposure; *d*, corpuscle with vacuolated nucleus and no pigment. × 450.

Coloured Blood-Corpuscles of Man.—The human coloured corpuscle is a convenient example of the non-nucleated red corpuscle. Viewed edgewise, it is flattened and biconcave (Fig. 16, *b*). When lying on its broad surface it has a circular shape (*a*), and, being biconcave, it has a shadowed centre surrounded by a light ring, or the reverse, according as the concave centre or the convex margin is brought into focus. It has a smooth surface, is transparent, and of a pale yellow colour. When withdrawn from the circulation the corpuscles usually run together into piles (*rouleaux*) (*c*).

The Effects of Reagents on Coloured Blood-Corpuscles of Newt and Man are important because of the indications they give of the structure and chemical composition of the corpuscles. Their effects will be better understood if it be previously stated that the coloured corpuscle has a thin, clear, soft, extensible, but perfectly elastic envelope, as indicated by Schwann, though many have erroneously disputed his statement. The pigment lies outside the nucleus, in the nucleated corpuscles,—and it is very generally believed that it fills the meshwork of a colourless, soft, elastic, thread-like (Hensen, *Op.* 38, vol. i. 409), or sponge-like (Brücke, Rollett, *Op.* 38, i. 410) stroma, that stretches from the envelope throughout the interior of the corpuscle. The existence of the stroma can scarcely be held as definitely proved, but it seems necessary to explain the persistent maintenance of a definite shape by the non-nucleated corpuscle.

Magenta solution reddens the nucleus of the *newt's* corpuscle, and also reddens one—rarely two minute swellings in the wall of the corpuscle. In the *human* corpuscle the latter is the only part that is stained (Fig. 22, *f*). The significance of this coloured macula in the envelope, discovered by Roberts (*Op.* 4, vol. xii. 481), is altogether obscure. The fact that it occurs in the nucleated, as well as in the non-nucleated corpuscle, prevents the supposition that in the latter it is to be regarded as a shrivelled nucleus.

Water.—When water is added to the newt's corpuscles, they lose their flattened shape, and become ovoid and sometimes spherical. This seems to be due to softening of the stroma and envelope, and to imbibition. The pigment may gather around the nucleus, but usually it diffuses into the surrounding fluid, leaving the corpuscle colourless. The nucleus may also swell up: sometimes it remains within the corpuscle (Fig. 19, *a*) or moves to the side, and becomes partially or completely discharged. In the latter case no rent remains in the envelope, probably because it is a colloid membrane, somewhat like that of a soap-bubble. Eventually the envelope may dissolve and disappear. When the *human* corpuscle is acted on by water it becomes spherical. The shadowed spot is therefore lost. The colour vanishes, and the corpuscle may eventually disappear.

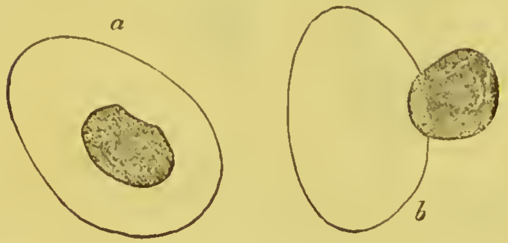

Fig. 19. Red blood-corpuscles of newt altered by water. *a*, Corpuscle with retained, *b*, with discharged, nucleus. × 800.

Dilute Alcohol (rectified spirit one part, water two parts, Ranvier) causes the newt's corpuscle to swell and lose colour. The nucleus also becomes enlarged, and a nucleolus is revealed. After this re-agent the envelope of the corpuscle—defined by a double contour—may be clearly seen with a high magnifying power, and it becomes specially evident after the addition of magenta. The human corpuscle when thus treated becomes spherical, colourless, and its envelope may then be clearly seen, especially if magenta be added (Ranvier, *Op.* 39, p. 187).

Dilute acetic acid causes the *newt's* corpuscle to *suddenly* distend, but its oval form is mostly retained. The pigment diffuses into the surrounding fluid, or, as Henle long ago observed, it may penetrate the nucleus and stain it yellow. Probably the acid softens the stroma and the envelope, and the sudden enlargement occurs when the endosmotic current is thus enabled to overcome the resistance to distension. If the corpuscles have been for some time removed from the body previous to the addition of the acid, the perinuclear portion may be seen to shiver into irregular masses, as if some coagulated substance had been ruptured (Fig. 20, *a*). When acetic acid is added to the *human* corpuscle it becomes spherical, and its pigment diffuses into the surrounding fluid. No nucleus appears.

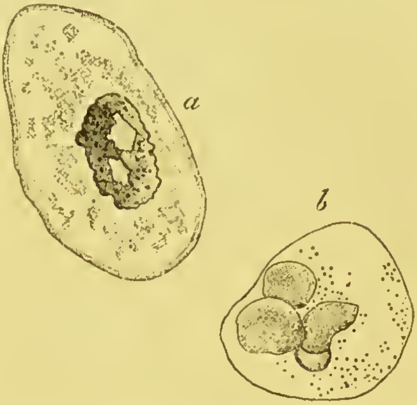

Fig. 20. Blood-corpuscles of newt after the action of dilute acetic acid. *a*, Coloured, *b*, colourless corpuscle. A single nucleus seen in the former, four in the latter. × 450.

Tannic acid (Roberts, *Op.* 4, year 1863) in dilute aqueous solution ($\frac{1}{2}$ per cent) if added to the *newt's* corpuscles *before their substance becomes set*, by what appears to be a process of internal coagulation, produces a remarkable series of changes. Imbibition takes place, and soon thereafter the hæmoglobin may be seen to withdraw itself from the interior of the envelope. It may gather as a stellate mass around the nucleus (Fig. 21, *c*), but usually it becomes partially or completely extravasated in the form of a bud (*a*, *b*), mostly single, but sometimes there are two, rarely three. The envelope of the corpuscle is ruptured, and its margin may sometimes be clearly seen constricting the bud (*a*). In some cases, however, no bud is formed, but the pigment particles spring out of the corpuscle in a diffuse fashion (*d*, *e*). In this case it is very evident that the extravasated substance at once coagulates and is precipitated, doubtless by the tannin, the moment it reaches the exterior of the corpuscle.

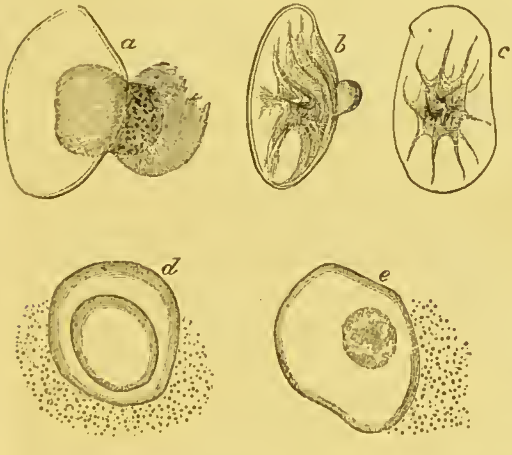

Fig. 21. Newt's coloured blood-corpuscles altered by tannic acid. *a*, *b*, Hæmoglobin extravasated in the form of a bud surrounded by a faint envelope in *a*. In *d* and *e* the surrounded pigment is extravasated in a diffuse form. In c it is gathered round the nucleus. × 400. (Reduced.)

Previous to the pigment extravasation, the nucleus often swells (*d*), but in other cases it undergoes no change in size.

This singular reaction may also be well seen in the human corpuscles (Fig. 22, *d*), where it often happens that each bud is enclosed in a delicate vesicular envelope that rapidly enlarges and may finally rupture from endosmosis. This hood to the bud is sometimes also seen in the newt's corpuscle (Fig. 21, *a*). A somewhat similar reaction is produced by a two per cent solution of boracic acid (Brücke, *Op.* 40, vol. lxvi. p. 79).

When magenta solution is added to the newt's corpuscles, after these buds have appeared under the influence of tannin, the buds become brilliantly stained. The same thing happens to the buds of the non-nucleated human corpuscle, and the change is very singular; for previous to the addition of tannin, the perinuclear substance of the newt's corpuscles is not stained by magenta. Dr. Roberts (*Op. cit.*) suggests that possibly the red blood-corpuscle has a double envelope, and that its contents may rupture only the inner one, while the outer of the two swells up and forms the hood over the bud. That a membrane is ruptured cannot be doubted, but whether the hood of the bud is a part of an outer membrane must be regarded as extremely doubtful, for it remains so adherent to the periphery of the bud.

A saturated solution of common salt or sugar causes the red corpuscles of both newt and man to become puckered from exosmose. Desiccation has a similar effect. When thus influenced, the corpuscles become crenated (Fig. 22, *c*), or spinous, like a horse-chestnut (*b*). Seen endwise, the spinous projections have the appearance of granules. In some cases, however, crenation cannot be so easily explained, for it is regularly produced in some animals, *e.g.* in the dog, in poisoning by Calabar bean (Fraser); and in this case it seems difficult, if not impossible, to ascribe it to a change of specific gravity, either outside or inside the corpuscles. Shocks of induced electricity may also render them spinous.

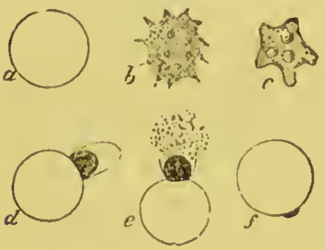

Fig. 22. Human red blood-corpuscles variously altered: *a*, by water; *b*, *c*, by short exposure to the air; *d*, *e*, by tannic acid; *f*, by magenta. × 1000.

Mechanical pressure can greatly distort and even rupture the corpuscles. The fact that no *shreds* of their envelopes are afterwards discernible has been adduced as an argument against the existence of such a membrane. But if, as already stated, the membrane be of a colloid nature, this circumstance would be explained. The completeness with which the corpuscles recover their shape, when relieved from the distorting influence of pressure, not too severe, seems only explicable by supposing not merely that the envelope is elastic, but also that there is an *elastic stroma* stretching from its interior throughout the corpuscle. It is particularly necessary to entertain this idea in the case of the non-nucleated red corpuscle, because of the persistence with which it recovers its shape after distortion.

These various reactions clearly show that the mammalian corpuscle behaves like the perinuclear part, and not like the nucleus of the nucleated corpuscle.

Actions of other Reagents.—Bile and salts of the bile acids (Kühne), ether (Wittich), chloroform (Böttcher), and alkalies dissolve the red corpuscles and liberate their pigment. Stricker (*Op.* 38, i. p. 404) has shown that when the newt's corpuscles have been slightly affected by water, a stream of CO_2 occasions a precipitate within them which disappears on exposure to a stream of oxygen. He agrees with Schmidt in supposing that the precipitable substance is paraglobulin (p. 36). Electrical discharges from a Leyden jar, or induction shocks, render the human corpuscles successively crenate, spinous, globular, and colourless. These effects are as yet unexplained. Electrolysis might be assigned as their cause; but the constant current, though much more electrolytic, does not produce the same effects (Rollett, *Op.* 38, vol. i. 390).

FORMATION OF ROULEAUX.—In a normal state of the blood, the red corpuscles exhibit no tendency to run into groups within the blood-vessels, but when the blood is shed, the red corpuscles, after the lapse of ten seconds or so, run together, and if they be the circular concave discs of mammalian blood, their clusters resemble piles of coin (*rouleaux*) (Fig. 15). The mutual cohesion of the corpuscles is not great, for they may be detached by even slight mechanical force. The following experiments devised by Norris (*Op.* 4, year 1869, p. 429) can be readily performed, and throw light on the question, why it is, that under one condition the corpuscles do not, while under another they do, run together.

(1.) Thin discs of cork are so poised with shotted pins, that when placed in water they float in a vertical position, and are only partially submerged. When a number of these are thrown into water, they—if the distances between them be not too great—quickly form rouleaux exactly like the blood-corpuscles. Their *running together* is due to *capillarity*—the result of their partial submersion, and their running into *rouleaux* results from their *shape;* for if spherical corks be employed, they form irregular clusters. (2.) When the corks are so weighted that they are totally submerged, they no longer run together; for capillarity is no longer in action, and gravity, operating between masses so small, is too feeble to produce any notable result. This second case is similar to the blood-corpuscles in their normal state within the blood-vesels. (3.) But if the cork discs wetted with *water* be submerged in *petroleum* (or conversely) *they form rouleaux;* apparently because there is cohesive attraction between the molecules of water on the neighbouring discs, and repulsion between the water and the petroleum. The formation of rouleaux by the red corpuscles of shed blood may be due to a change in the corpuscles, or in the plasma, whereby their physical relations become analogous to those between the wetted corks in petroleum.

It is certain that some important change occurs in the coloured corpuscles within a few seconds after their removal from the blood-vessels. They seem to coagulate (p. 59). Their elasticity after a time diminishes, and they become somewhat viscous. It may therefore be, that owing to some change in the surfaces of the corpuscles they cease to attract, or it may be they even tend to repel the surrounding fluid—while they attract one another. It may be, however, that the phenomenon results from some change in the *liquor sanguinis.*

Rouleaux are not formed by red corpuscles that are nucleated, for although they run together under the conditions detailed above, their shape allows of adhesion in irregular clusters only.

CHEMISTRY OF THE RED BLOOD-CORPUSCLES.—The red blood-corpuscles contain water, solids, and gases. There is rather more water than solids. The solids—almost entirely organic—are chiefly haemoglobin and paraglobulin. Lecithin and cholesterin also occur in small amount. Hæmoglobin is an albuminoid matter (p. 37) that forms a loose compound with oxygen in the lungs, which it yields up at the systemic capillaries, and thus acts as the chief carrier of oxygen from the lungs to the tissues. In virtue of this property of hæmoglobin, the coloured blood-corpuscles are agents essential for the maintenance of the respiration of the tissues. The *stroma* of the corpuscles is believed to consist of proteid matters of which but little is known. They belong to the globulin group. Paraglobulin, a substance that can be precipitated by carbonic acid, and redissolved by oxygen, is one of them. The salts of the corpuscles are principally potassium chloride and potassium phosphate. The salts of the red corpuscles and of muscle notably differ from those of other tissues in the fact that sodium salts are almost entirely replaced by those of potassium. The principal gas of the corpuscles is oxygen, but they also contain a trace of carbonic acid.

The quantities of the chief constituents are as follows:—Water, 56·5 per cent. Solids, 43·5. 100 parts of the *dried organic matter* of the corpuscles of dog's blood (Jüdell, *Op.* 21, Heft iii. 386) contain hæmoglobin, 86·5. Other albuminoid matters, 12·55. Lecithin, 0·59. Cholesterin, 0·36.

Development of Blood-Corpuscles.—In the embryo the blood-corpuscles are developed exclusively in the *middle* layer of the germinal membrane.

In the chick, according to Klein (*Op.* 40, year 1871), the blood-corpuscles are developed from the nucleated protoplasts of the mesoblast in two ways—(1) The nuclei of certain protoplasts multiply, and the polynucleated mass differentiates into a central mass of nucleated protoplasts—young blood-corpuscles (*d* in large central mother-cell of Fig. 23); while the outer part becomes an envelope—the wall of a future capillary—consisting of a nucleated layer of protoplasm (*b* in same cell). The protoplasmic wall of the capillary grows outwards at various points (B_1), and joins processes (*f*) from neighbouring cells. The processes, at first solid, become hollow, the blood-plasma appears between the blood-corpuscles, and thus a system of capillaries and vascular contents arise. (2) Another and perhaps more frequent mode of formation consists in an *early vacuolation* of the polynucleated protoplasmic mass (*B*). The vacuole (*a*) is the interior of a future vessel, and is filled with blood-plasma. The nuclei in the vascular wall proliferate, and with some of the protoplasm grow as buds towards the interior of the vessel, drop off, and become blood-corpuscles (*d*). While this is going on, the protoplasmic wall of the mother-cell buds outwards, branches, joins with the processes of its neighbours, and forms a system of capillaries in the way already described, its polynucleated protoplasm becoming a series of epithelial plates, that constitute the wall of the capillaries.

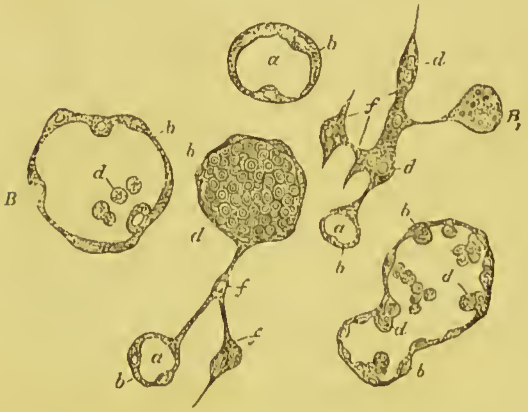

Fig. 23. Development of blood-vessels (*b*) and blood corpuscles (*d*) in mesoblast of chick. See text. (Klein.)

Klein asserts that the blood-pigment appears in the protoplasm around the nuclei of the coloured corpuscles; but Balfour (*Op.* 8, xiii. p. 280) maintains that the perinuclear pigmented parts of the blood-corpuscle are formed from the nuclei of the parent cell, while the nucleoli of the latter become the nuclei of the blood-corpuscles.

Blood-vessels and also blood-corpuscles may originate in a manner similar to the above in inflamed tissues (Stricker, *Op.* 38, iii. p. 542).

After the development of blood-corpuscles and blood-vessels the former multiply during a considerable period of early embryonic life by fissiparous division, as Remak first pointed out.

In mammals the blood-corpuscles probably arise in a manner analogous to that observed in the chick. Precise information, however, is wanting. But, at all events, the primitive red blood-corpuscles are nucleated in all mammals as they are in other vertebrates. All the corpuscles are at first colourless, nucleated, granular protoplasts, but ere long many of them lose their granules and become coloured by pigment that appears in the perinuculear portion (Kölliker). Balfour (*lib. cit.*) is, however, inclined to suppose that the *nucleus* of the mammalian corpuscle is an *enlarged nucleolus*, while the *nucleus becomes pigmented* and forms the outer part of the corpuscle, as Wharton Jones, Busk and Huxley long ago maintained (compare p. 60). The nucleated red corpuscles are spherical, relatively large, and multiply by fission (Fig. 23A) occurring throughout the entire mass of the blood until that period of development at which the liver appears, when the formation of the coloured corpuscles by fission comes to an end. Up to this point the coloured corpuscles are therefore produced in two ways—(1) from white blood-corpuscles, (2) by fissiparous division of themselves.

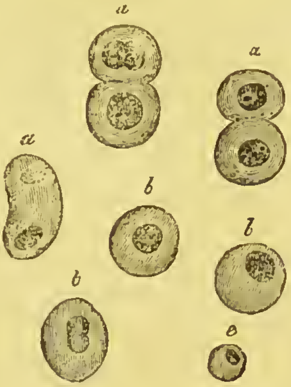

Fig. 23A. Coloured blood corpuscles of embryo sheep 3½ lines long. *a*. corpuscles dividing; *b*, corpuscles showing division of nucleolus, and incipient division of nucleus; *c*, a small corpuscle. (Kölliker.)

Great obscurity hangs over the development of the coloured corpuscles after the appearance of the liver and blood-glands. All are agreed that the young colourless blood-corpuscles (lymph-corpuscles) are developed throughout life in the spleen, lymphatic, and other blood-glands; and probably no one doubts that throughout life, as in the early embryo, the coloured corpuscles are derived from the colourless ones. It is supposed that the transition of the one into the other takes place in the spleen, in the lymphatic glands or lymph, and in the embryonic liver; but although Paget, Kölliker, and others maintain that the white corpuscle becomes flattened, loses its nuclei, and acquires colour, while Wharton Jones, Busk, Huxley, Gulliver, and Balfour assert that the nucleus is the portion which becomes pigmented and forms the red corpuscle, it must be admitted that the whole question is still obscure, and it may be doubted if the transition has ever been fairly observed in mammals at a period later than early embryonic life. Kölliker (*Op.* 45, p. 534) suggests that the difficulty in the case may possibly be owing to the transition taking place rapidly. Further details regarding the development of blood-corpuscles must be postponed until the subject of blood-forming glands is under consideration; but before leaving the subject it may be well to return to the cellular morphology of the blood-corpuscles, and now, since their development has been described, to repeat that while the white corpuscle is a nucleated protoplast, the red corpuscle of the fish, amphibian, and bird, is a nucleated periplast. The mammalian corpuscle, whether developed from the perinuclear protoplasm or the nucleus, is a periplast devoid of all the properties of protoplasm and of nuclei.

NUMBER OF CORPUSCLES.—In *relative* number the red are much more numerous than the white corpuscles. In the blood generally, the colourless are in the proportion of 1 to 500 of the coloured (Malassez, *Op.* 13, year 1872), whilst in the blood of the splenic vein the proportion is stated by Hirt to be 1 to 70. In ordinary conditions only three or four colourless corpuscles are to be detected in the field of the microscope, but in certain pathological states, such as *leucocythæmia*—dependent on enlargement of the spleen or lymphatic glands—the colourless corpuscles are greatly increased in number.

The *absolute* number of the coloured corpuscles has been estimated by Welcker, and more recently by Malassez (*Op.* 11, year 1877, p. 634). A cubic millimeter of blood contains 5,000,000 coloured corpuscles. In certain diseases the corpuscles undergo a marked variation in number; thus in anæmia, the number may fall to 800,000 per cubic millimeter. Malassez has shown that the administration of iron has a marked effect on the number; within a few days after the administration of the iron there is usually a great increase in the number of the coloured corpuscles.[1]

FUNCTIONS OF THE CORPUSCLES.—The *red* blood corpuscles are chiefly concerned in carrying oxygen from the lungs to the tissues. The oxygen is loosely combined with their colouring matter—the hæmoglobin. The relations of this substance will, however, be studied afterwards. The fact that all the red corpuscles are not affected to the same degree by some re-agents—*e.g.* by water, tannin, etc.—shows that they in some respects differ from one another in physical, and perhaps in chemical, composition. Probably the difference is due to age, for it cannot be doubted that the red are produced from white corpuscles in the spleen and elsewhere, and that, after existing for a time in the blood, they break up and disappear in the pulp of the spleen, and possibly in other parts. This subject will be elsewhere discussed in detail, but it may be added here that very possibly some of the substances resulting from their disintegration are used as nutritive elements throughout the economy. This point, however, is still very obscure. The *white* produce the coloured corpuscles. In the embryo, and in certain pathological conditions, they can emigrate from the vessels and take part in the formation of various tissues.

The Granular Elements of the Blood.

The so-called granules of the blood are (*a*) minute particles of protoplasm (Fig. 16), first detected by Beale. Their origin is obscure, but some of them, at all events, are probably fragments of protoplasm detached from the white corpuscles. (*b*.) Fatty particles are always detectable in the blood during digestion. In sucking infants they are always present in such numbers that the serum is milky.

LYMPH CORPUSCLES.

As already stated, these are young white blood-corpuscles, and they will be specially alluded to under Blood-Glands and Lymphatics.

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[1] A description of Malassez's method of enumerating the blood-corpuscles is given in the author's *Practical Histology*, 2d edition, p. 62.

CHAPTER VII.

EPITHELIUM.

Epithelium consists of cellular units of great importance in the economy. It constitutes a protective covering for the skin and mucous membranes. In synovial and serous membranes it forms a smooth polished surface, whereby the friction of solids and fluids is reduced to a minimum. It is the secreting element of all the glands of the body, save blood-glands; and in the nose, mouth, and ear it is modified into special terminal organs for the nerves of sense. A tissue formed of elements that are comparatively simple and often similar, but with functions so varied, constitutes a singularly interesting subject for physiological study.

Mucous membranes line the alimentary and respiratory canals, genito-urinary passages, lachrymal apparatus, middle ear, and Eustachian tube. These cavities all directly or indirectly open externally, and their lining membrane secretes a viscid fluid termed mucus.

Synovial membranes are found in joints, bursæ-mucosæ, and around some tendons, and are lubricated by a viscid fluid termed synovia.

The principal *serous* membranes are the peritoneum, pericardium, pleura, and the arachnoid. They contain some serous fluid that permits of an easy movement of their apposed surfaces—a matter of much importance in the thorax and abdomen.

Epithelium is developed from cells in all three layers of the blastoderm. The epithelium of the skin, mouth, nose, and pharynx, cavities of the brain and spinal cord, is derived from the *epiblast;* that of the alimentary canal and its glands below the pharynx, the lungs, and the urinary bladder, is derived from the *hypoblast;* while the *mesoblast* gives rise to the epithelium of blood-vessels, lymph-vessels, serous and synovial membranes, kidneys, ureters, testes and their ducts, ovaries, Fallopian tubes, and uterus.

Epithelial Cells vary in size from 25 to 83 μ ($\frac{1}{1000}$ to $\frac{1}{300}$ inch). They are mostly colourless, but in certain regions, such as the deeper layers of the epidermis, that is, the epithelium covering the skin, they contain pigment. Their shapes are mostly polygonal, rarely spheroidal, because the cells as they grow press one against another. The full-grown cells may be scales, cylinders, cubes, or their forms may be indefinite. They have usually one, but sometimes they have two nuclei. In many situations the cells appear to be cemented together by a small quantity of a colourless interstitial substance, and they are disposed either in one or in several layers, the former arrangement being termed *simple*, the latter *stratified* or *laminated.*

Epithelial cells have been classified according to their shapes, but as these are so varied, it is impracticable to adopt this as the sole basis of classification. It is, therefore, advantageous to have regard to their *function* as well as to their *form*, and on this ground five chief varieties may be recognised—1. *Squamous;* 2. *Columnar;* 3. *Transitional;* 4. *Ciliated;* 5. *Glandular.* Although it must be admitted that these divisions are somewhat arbitrary, they are nevertheless convenient.

SQUAMOUS EPITHELIUM.

The fully-formed cells of squamous (scaly, pavement or tesselated) epithelium are thin more or less polygonal plates (Fig. 24, *a*). Their shapes are usually irregular, but on the outer aspect of the retina they are hexagonal.

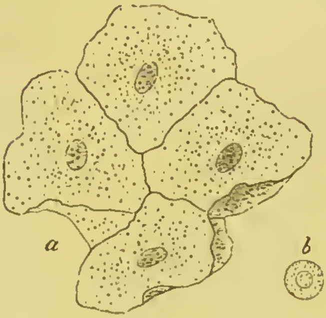

Fig. 24. *a*, Squamous epithelial cells from interior of mouth: *b*, salivary corpuscle. × 300.

Stratified Squamous Epithelium covers the skin, alimentary canal above the stomach, the anterior surface of cornea, the conjunctiva, the vagina, and the lower half of the cervix uteri. The life-history of the cells may be traced in a thin vertical section of the human epidermis, after hardening in dilute chromic acid (Fig. 25). The cuticle consists of two principal layers of cells—the *horny layer* (A) placed externally, and beneath this a soft layer, the *rete mucosum* (B). The cells proliferate in the deeper layers of the rete mucosum (*a*). Evidence of this proliferation is to be found in the fact that the nuclei usually contain two or more nucleoli, and may themselves be found constricted and evidently about to undergo division (*a'*). The division of the general cell-substance, however, is much more difficult to detect, for a reason afterwards to be explained, while the cells are being pushed outwards by the multiplication of those below as they grow larger. The protoplasm becomes converted into a dense horny periplast (*b*). The nucleus may remain or may disappear. The superficial horny scales are gradually detached by friction; hence the necessity for the production of new cells in the deeper layers to replace them. Stratified squamous epithelium is found on all surfaces that are much exposed to friction.

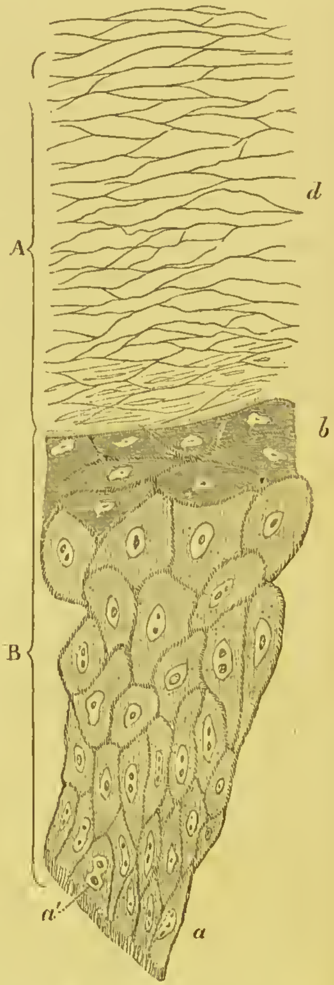

Fig. 25. Vertical section of cuticle of finger. A, Horny layer; B, *Rete mucosum*. *a*, Youngest cells; *a'*, a nucleus dividing; *b*, uppermost cells of rete mucosum; *d*, old scales of horny layer. × 300. (From a preparation hardened in chromic acid and stained with picrocarmine.)

Spinous or Prickle Cells.—In the lower layers of stratified squamous epithelium the cells have a denticulate appearance (Fig. 25, *a*, and Fig. 26). The apparent spines of neighbouring cells are not interlocked, as Max Schultze maintained, but are continuous at their apices as Martyn (*Op.* 9, xvi. p. 59) pointed out. This may be seen in a vertical section of epidermis, after hardening in osmic acid by the method described by Ranvier *Op.* 39, p. 261). The acid darkens the cell-substance and thus reveals the contour of the cell marked by a line of rounded spaces (Fig. 26), between which the so-called "prickles" stretch as bridges between the cells. The prickles seen on detached cells apparently result from the rupture of these bridges by mechanical methods employed for isolating the cells.

The spaces between the bridges are probably channels through which the lymph permeates from the subjacent capillaries to nourish the growing cells of the *rete mucosum.* There is, however, no escape of lymph through the epidermis, owing probably to the cells of the upper layers being horny and closely matted together. The division of the cells in the lower layers appears to be indicated by nothing more than the formation of vacuoles along certain lines. Hence the difficulty in detecting the cells in the act of dividing.

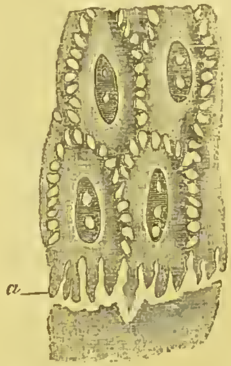

Fig. 26. So-called "prickle" cells from lowest layers of epidermis of finger, after staining with osmic acid. *a*, Processes of cells dipping into fibrous layer of skin. × 1000.

SIMPLE SQUAMOUS EPITHELIUM OR ENDOTHELIUM[1] lines serous and synovial membranes, blood and lymph vessels, air vesicles, posterior surface of cornea, and outer surface of retina. In the last situation the cells are hexagonal, but elsewhere they are irregular in shape. In lymphatics their outlines are remarkably sinuous. It is always difficult to see their outlines unless they are darkened by the silver process, in which the fresh epithelial surface is treated for two or three minutes with a dilute solution of silver nitrate. After exposure to light, dark lines appear mapping out the margins of the cells. These *silver lines,* as they are termed,

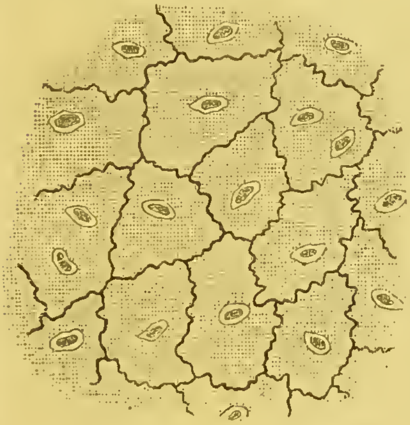

Fig. 27. Simple squamous epithelium or endothelium of frog's mesentery. Silvered. × 300.

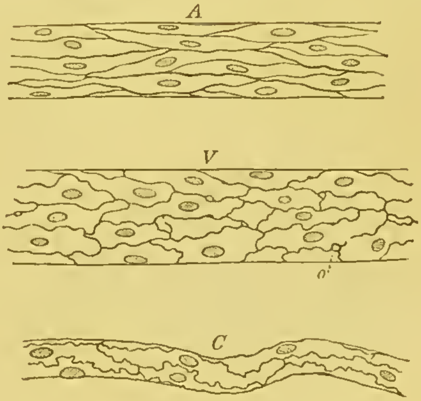

Fig. 28. Endothelial lining of *A*, artery; *V*, vein; *C*, capillary. Silvered. × 300.

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[1] The term *endothelium* was applied by His to the epithelium derived from the mesoblast, but only confusion resulted from the use of a term that thus included the simple squamous epithelium of the vascular system, the secreting epithelium of the kidney and testis, the ciliated epithelium of the uterus, and the irregular transitional epithelium of the ureters. The term is, however, a convenient one if it be merely used as synonymous with *simple squamous epithelium,* and applied to that *irrespective of its embryonic origin. In this sense only* it will be employed throughout this work.

are due to a reduction of the silver salt in what appears to be an interstitial or cementing substance. Prolonged action of the silver solution, however, is followed by darkening of the general cell-substance as well as of the cement. We owe to His and Recklinghausen this method which has already proved of great value in the study of blood-capillaries and the lymphatic system.

Endothelial plates are probably all nucleated at an early period of development, and the nucleus is often permanent, but it disappears from many cells as they grow old (Fig. 29, *c*). The duration of endothelial scales and the mode in which they are replaced are points of much obscurity. In the air-vesicles small nucleated finely-granular cells (Fig. 29, *b*), apparently of a germinal character, may be seen at intervals amidst the large clear plates, and though division of the small cells may sometimes be seen (*b*), it is doubtful whether or not they expand and replace the large ones. In blood-vessels, however, these minute germinal cells are wanting, and nothing can be seen but a layer of clear plates similar to the larger scales in the air vesicles, but mostly nucleated.

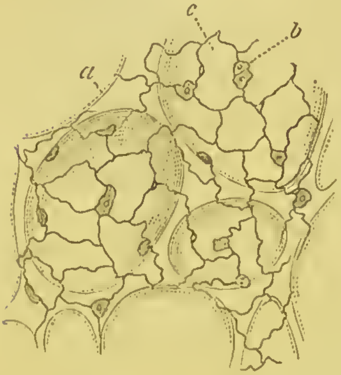

Fig. 29. Silvered endothelium of vesicles of lung of cat. *a*, Outline of air-vesicle; *c*, old endothelial scale; *b*, nucleated finely-granular cells. × 300.

COLUMNAR EPITHELIUM.

Columnar epithelium lines the alimentary canal below the œsophagus, and the greater part of the ducts opening into the canal, including the gall-bladder. It is also found in the olfactory region of the nose, in the urethra, and *vas deferens*. It exists everywhere as a single layer,

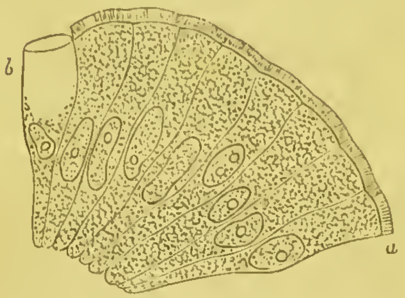

Fig. 30. Columnar epithelium from small intestine of cat. *a*, Striated border at free end of cell. *b*, Chalice cell. × 600.

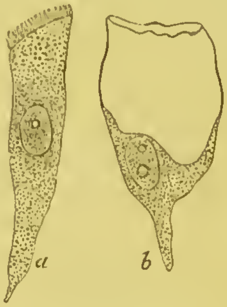

Fig. 31. Fresh epithelium from cat's large intestine, after magenta staining. *a*, Ordinary columnar cell with border split up by artificial pressure. *b*, Chalice cell. × 600. (The two cells are in exact relative proportion.)

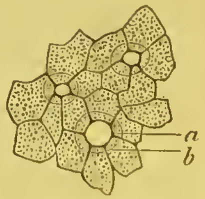

Fig. 32. Surface view of free ends of columnar epithelium from villus of frog's intestine, silvered. *a*, Opening of chalice cell. *b*, Periphery of the broader subjacent part of the cell. × 400.

except in the urethra, where it is stratified. The cells are set endwise on the membrane which they cover. They may be of tolerably uniform calibre, but usually they taper towards their attached extremities, which may be single (Fig. 31) or branched. The cells are laterally compressed, so that a superficial view of their free ends resembles a mosaic (Fig. 32). The cells are mainly composed of granular protoplasm, usually with a single nucleus. In the intestine there is a clear band at the free end of the cell (Fig. 30, *a*). This clear hem is traversed by fine vertical striæ. Whether these are fine pores or the outlines of minute rods it is difficult to determine. When the cells are subjected to pressure during preparation, the striated border sometimes splits up and becomes serrated (Fig. 31, *a*). Magenta stains the general cell-substance but not the hem, which, together with a delicate cell-membrane, seen at all events in the chalice cell (Fig. 31), may be regarded as the periplast. When fresh columnar epithelial cells are placed in water, clear blebs speedily appear at the broad ends of the cells, consisting of mucin swollen up by endosmose. Mucin is therefore produced in the ordinary columnar cells.

CHALICE (GOBLET OR CUP) CELLS are found on mucous membranes amidst columnar and ciliated epithelial cells. They are numerous in the small, but particularly so in the large intestine. They may be easily obtained from the *fresh* large intestine of the cat, by simply scraping the epithelial surface and staining with magenta, which reddens the nucleus, and the small quantity of protoplasm usually found near the attached end of the cell. At the free extremity there is an open mouth that communicates with a large cavity in the interior. These chalice cells may be about the same size, but *usually they are larger* than the columnar cells (Fig. 31).

There has been considerable discussion regarding the precise nature of these cells, it being maintained, on the one hand, that they are merely old cells undergoing mucin transformation and breaking down; and on the other, that they are unicellular glands for the secretion of mucin. The former idea receives support from the fact that when a piece of intestine is macerated for some weeks in a dilute solution of chromic acid, the striated hem falls away from many of the cells, the protoplasm becomes vacuolated, and the cells are not unlike the normal chalice cell. On the other hand, the latter is *usually larger* than the columnar cell. It almost always has a nucleus with some protoplasm, and after careful staining with logwood a plug of mucin may often be seen projecting from the mouth of the cell. It seems difficult to explain these facts, especially the larger size, on the theory that they are old cells breaking down. It is more likely that they are unicellular mucin-forming glands, as F. E. Schultze suggested (*Op.* 18, iii. p. 137).

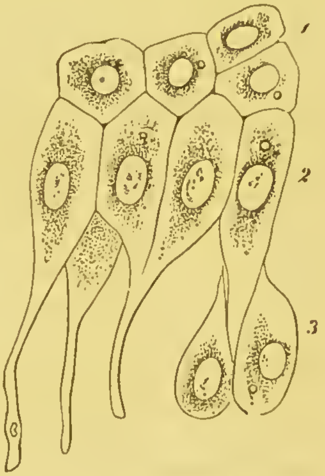

Fig. 33. Transitional epithelium from urinary bladder. 1, Cells at free surface; 2, cells in middle; 3, cells in deepest layers. (Obersteiner.)

TRANSITIONAL EPITHELIUM.

This term was applied by Henle to the epithelium of the urinary bladder, ureter, and pelvis of the kidney. The cells are stratified, and of various shapes. They may be squamous, columnar, cubical, or altogether indefinite. On the whole, however, they are a sort of *transition* between the squamous and columnar form.

CILIATED EPITHELIUM.

Ciliated epithelium lines the respiratory passages,—*viz.* the lower part of the nose, the upper part of the pharynx, the larynx, trachea, and bronchi. It is also found in the cavities of the brain and spinal cord, in the tympanum, Eustachian tube, Fallopian tube, and uterus above the middle of the cervix. In the respiratory passages, excepting the finest bronchi, the cells are stratified. In other situations there is only a single layer. The cells are mostly columnar. Their attached ends are more or less pointed, and at their free extremities there is a brush of fine cilia planted on a clear band. The general body of the cell is composed of a nucleated finely-granular protoplasm. In the stratified arrangement of this epithelium only the upper layer of cells is ciliated. The cells proliferate in the deepest layers, gradually elongate, reach the free surface, and become ciliated. Regarding the development of the cilia, however, definite information is still wanting.

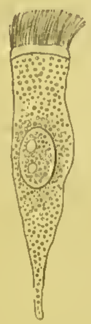

Fig. 34. Ciliated epithelial cell from trachea. × 600.

The cilia are flattened filaments tapering towards their free ends, and about 8 μ ($\frac{1}{3200}$ inch) in length (Fig. 35). They consist of a colourless and *optically* homogeneous material, that appears to be continuous with the substance of the clear band. If, however, the cells be placed for twenty-four hours or so in one-fifth per cent solution of osmic acid, it may be seen that the cilia pass through the clear band and are continued for a very short distance into the protoplasm. The cilia cannot be regarded as consisting of ordinary protoplasm, for they are elastic, they preserve a definite shape, and contract in a definite way, and further, they are not stained by carmine or magenta. Yet, like protoplasm, they chiefly consist of proteid material, like many forms of protoplasm they are contractile,—although in this more highly organised structure the contractions differ from those of undifferentiated protoplasm,—and they are continuous with the cell protoplasm. Their very close alliance to ordinary protoplasm may therefore be indicated by describing them as consisting of modified protoplasm.

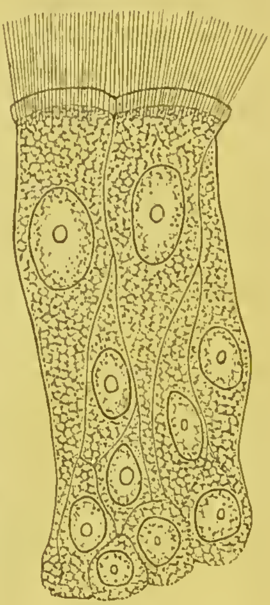

Fig. 35. Stratified ciliated epithelium from trachea of cat, after treatment with osmic acid. × 1200.

CILIARY MOTION may be readily studied in the gill of the salt-water mussel, for there the cilia are much larger than in the vertebrata, and the ciliary motion continues for a considerable period after a portion of the gill has been detached. The cilia must be moistened with *sea water*, for fresh water quickly paralyses them. The living cilia have a rapid lashing movement by which the surrounding fluid is thrown into a stream. When their movement slackens in speed previous to death, it may be observed—

in the large cilia on the mussel's gill—that each cilium simply bends during contraction and then straightens itself, and as they die, they tend more and more to remain erect. The act of bending is therefore a vital phenomenon, and is ascribed to contractility.

As the cilium does not shorten like a muscular fibre, but merely bends, we are obliged to conclude that one or more bands of contractile substance run along one side of the mesial plane, and it is probable that there is an elastic band on the other side, whereby the cilium is brought back to its erect position. This inference as to structure, deduced from the manner in which they move, receives support from the fact that the large cilia of bivalves may—by pressure—be split up longitudinally into two, or sometimes indeed into a bundle of fibrils.

The fluid around the cilia is moved in the direction in which they bend, and the definite direction of the current may be explained by supposing that their *contraction* takes place with *greater velocity* than their *relaxation*. It has been supposed that the cilium when it relaxes partially rotates, and so moves back edgewise through the water, after the fashion of a feathered oar. But as no such thing can be seen, the former explanation, being in accordance with the visible event, is preferable.

A ciliated cell in the vertebrata, and at all events in most of the invertebrata, is an *automatic motor apparatus* (see p. 25). That it is independent of nerves is shown by the fact that detachment of the cell from its surroundings does not affect the ciliary motion. All the cilia on the same cell move simultaneously; from which it may be inferred that the impulse to movement springs up, not in the cilia individually, but in the cell. The *nucleus* of the cell is not essential for the movement, for the cell may be torn across between the cilia and the nucleus, and yet their movement continues, but if the cilia be detached from the end of the cell they are paralysed. This may be due to laceration of their contractile bands, or to their detachment from the cell protoplasm, in which the excitement probably originates. The movement travels in quick rhythmical order from one cell to another, but the manner in which the cells are *co-ordinated* so that a physiological continuity exists between them, permitting of the extension of excitement from cell to cell, is unknown. Ciliary movement is so rapid that its rate has not been precisely ascertained. In the frog,—when the cilia are in full activity the rate is at least twelve contractions per second (Engelmann, *Op.* 1, iii. 424). Gentle *heat* accelerates the movement: doubtless by accelerating chemical change. The effect of heat may be readily demonstrated on the mussel's gill after the speed of the ciliary motion has slackened somewhat. Elevation of the temperature to 45° C. (113° F.), in cold-blooded animals occasions rigidity with acidification, as happens in muscle under like circumstances. *Chloroform* vapour retards and then arrests ciliary movement (Lister, *Op.* 3, year 1858). On exposing the cilia to the air after their arrest by chloroform, their movement is resumed, if the chloroform has not acted too long. This may be explained by supposing that the molecules of chloroform diffuse into the contractile matter, and *inhibit* or restrain the chemical changes that produce mechanical movement; but the moment the tension of the chloroform outside the cilia is diminished by exposing them to pure air, the chloroform molecules escape by diffusion, leaving their material free to move as before. But after the prolonged action of chloroform the motion is not resumed, probably owing to some fatal chemical change in the protoplasmic machinery. The important bearing of this experiment on the effect of anæsthetics on nerve cells is obvious. Oxygen is consumed by contracting cilia. Kühne proved this by placing living ciliated epithelium in a solution of oxyhæmoglobin, and finding that after some time the hæmoglobin was reduced, owing to removal of its loosely combined oxygen. Oxygen is indispensable for the maintenance of the movement, for although the cilia may continue to contract for a considerable time in its absence, they certainly become paralysed unless it is supplied.

Carbonic acid first accelerates, and then arrests, the movement. The acceleration is probably owing to its exciting the cell, while the arrest is doubtless owing to a poisonous effect. A very dilute solution of caustic potash accelerates the motion when the cilia are becoming sluggish, and it may even recall the movement after it has ceased (Virchow). Dilute acids, and dilute alcohol, have also a reviving power. Observations on the effects of induced and of galvanic electricity have led to no perfectly clear results.

FUNCTIONS OF CILIA.—In the respiratory passages cilia discharge the important function of moving mucus out of the lungs into the pharynx, where it is swallowed. Cilia also remove mucus from the tympanum, and impel it into the pharynx; whilst in the Fallopian tube they aid in the downward passage of the ovum towards the uterus.

The Energy of Ciliary Motion is, as Wyman first showed, by no means inconsiderable. Elaborate experiments have been made by Bowditch (*Op.* 47, August 10, 1876) on this subject. His experiments were performed by removing the ciliated membrane of the frog's mouth, and fixing it on a plate of glass, with the ciliated surface free. The preparation was then placed on an inclined plane, different weights were applied to the ciliated surface, and the extent to which in a given time the cilia carried a given weight up the inclined plane was observed. He in this way ascertained that the cilia on 1 square centimeter of mucous membrane can perform in one minute 6·8 grammillimeters of work; that is, they can do work equivalent to raising 6·8 grammes to the height of 1 millimeter in one minute. He calculates that in one minute they could lift their own weight to the height of 4·25 meters. When compared with the work of a muscle, this is a relatively small amount of work for a contractile tissue to perform. It is little more than $\frac{1}{30}$ of the working power of the heart, which in one minute does work equal to lifting its own weight to the height of 150 meters (Schiff, *Op.* 48, i. p. 24).

GLANDULAR EPITHELIUM.

Epithelium is the secreting element in all glands save blood-glands. The term spheroidal has been applied to glandular epithelium, but the cells are usually polygonal—rarely spheroidal. They are nucleated protoplasts, usually without an envelope, so that the products of secretion readily escape. If chalice cells are to be regarded as unicellular glands (p. 68), they have an envelope, but there is a free opening at one end of the cell to allow the secretion to escape. Many of the substances found in secretions are produced within the gland cells; thus pepsin is formed by the gastric glands; the bile acids produced by the liver are not found in the blood, but are elaborated from the proteids of the blood by the glands. On the other hand, in such a gland as the kidney, the great function of the cells appears to be to withdraw from the blood matters already formed,—urea, etc.

Modifications of Epithelium.

Epithelial cells may be variously arranged and variously modified, to constitute hair, nail, hoof, horn, feather, fibres of the crystalline lens, enamel fibres of the teeth, and special cells forming the peripheral terminal organs of the nerves of smell, taste, and hearing.

CHEMISTRY OF EPITHELIUM.

The chemistry of epithelium is very imperfectly known. The young cells chemically resemble protoplasm in general, and contain glycogen (p. 40)—a starch-like substance—whose presence is revealed by iodine, which strikes an acacia-brown colour when glycogen is present. The old horny cells of squamous epithelium consist of *keratin* or *horny stuff* (p. 37), an albuminoid substance. They swell up in cold and dissolve in hot solutions of caustic alkalies. The soft feeling of the skin, after contact with alkalies, is due to this change.

The epithelial cells covering the retina, those of the hair, and those of the lower layers of the epidermis, contain a dark-brown pigment—*melanin* (p. 39).

Fat occurs in the epithelial cells of the sebaceous glands, and in those of the mammary glands during the secretion of milk. In the latter it appears from experimental data, afterwards to be detailed, that the fat is not simply withdrawn from the blood but is produced from proteids by the protoplasm. The fat flows away from the cell, and does not appear to encumber it. But in the cells of the sebaceous glands fat appears, accumulates in the cell, and becomes substituted for the protoplasm which vanishes. This substitution of fat for tissue elements is termed *fatty degeneration*, a common pathological change chiefly observed in protoplasm and its near modifications.

MUCUS.

Mucus is the colourless viscous fluid that moistens mucous membranes. It contains the débris of shed epithelium, mucus corpuscles, and mucin.

Mucus Corpuscles (Fig. 36) are nucleated masses of protoplasm, similar in size to white blood corpuscles ($12 \cdot 5\ \mu$), ($\frac{1}{2000}$ inch). Unlike the majority of white blood corpuscles, they generally possess a single globular nucleus, sometimes, however, there are two or three. In the normal mucus corpuscle taken, *e.g.*, from the human pharynx, or from the fresh trachea of a rabbit, the protoplasm exhibits even at the ordinary temperature amœboid movement, that becomes still more active when the corpuscles are kept at 38° C. (100° F.) Often the pseudopodia consist of hyaline protoplasm (Fig. 36). In the urine, mucus corpuscles are motionless, probably because their protoplasm is paralysed by the urinary constituents. Mucus cells are probably modified epithelial cells. Probably they are principally produced in mucous glands. The *salivary corpuscles* (Fig. 24, *b*) resemble them in size and in general appearance, and also in their usually containing a single nucleus. But they have no amœboid movement. There appears to be a thin envelope to the salivary corpuscle, between which and the nucleus there is a fluid in which granules exhibit Brownian motion. The origin of the

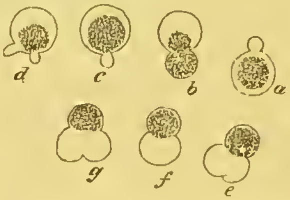

Fig. 36. Mucus corpuscle from human pharynx, examined at the ordinary temperature. The shapes from *a* to *e* were successively assumed in the course of ten minutes. × 300.

salivary corpuscles has not been fully ascertained, but the evidence is in favour of their origin from certain cells in the salivary glands.

MUCIN is an albuminoid substance (p. 37) that occasions the viscosity of mucous fluids. It is not coagulated by heat, but is precipitated by alcohol and by acetic acid, and the precipitate is not soluble in excess of the acid. The precipitate swells up in water, but does not dissolve in it; it is, however, readily soluble in alkalies. Mucin is largely produced in mucous glands. It is also formed in the ordinary secreting cells of the salivary glands, especially in the submaxillary and sublingual. That it is produced in the cells of ordinary columnar epithelium has been already stated.

The production of mucin in chalice cells has been already referred to. Mucin is useful because of its viscosity. It thereby facilitates the passage of matters such as the food over mucous surfaces. It is, however, an entirely excrementitious substance, and is therefore thrown out of the economy.

RELATIONS OF EPITHELIUM TO SUBJACENT STRUCTURES.

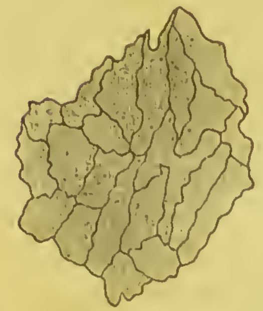

Fig. 37. Membrana propria from villus of cat's intestine. Silvered. × 300. (The nuclei are not shown by the silver process.)

BASEMENT MEMBRANE.—It was formerly supposed that on every epitheliated surface a homogeneous membrane, termed a *basement membrane* or *membrana propria* (Bowman), lies immediately beneath the epithelium. Such a membrane certainly exists in the kidney, alimentary canal, respiratory passages, bladder, and sweat glands. In the tubules of the kidney it appears to be homogeneous, but in the alimentary canal it can, by the silver process, be shown to consist of nucleated endothelial plates (Fig. 37) as pointed out by Debove (*Op.* 11, year 1874, p. 19). It lies immediately under the columnar epithelium, and may be revealed by brushing away the columnar cells and silvering the subjacent structures.

NERVES.—In the *rete mucosum* of the skin, on the anterior surface of the cornea, and on the tongue, nerves have been traced to epithelial cells, amidst which the nerve fibrils form plexuses. A structural continuity between nerve fibrils and ordinary epithelial cells has, however, not yet been satisfactorily demonstrated. In the case of the so-called "auditory" cells found in the ampullæ of the ear, Max Schultze demonstrated that the nerve fibrils are continous with the cells, an observation which has been

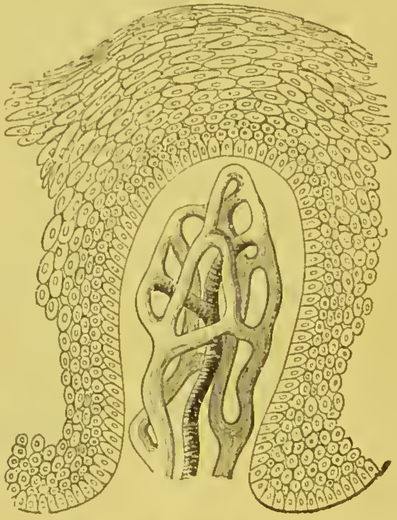

Fig. 38. Vertical section of a child's gum, showing the stratified epithelium covering a papilla with its blood-vessels. The connective tissue between the vessels and the epithelium has been omitted. × 250. (Todd and Bowman.)

confirmed. Such a connection, no doubt, also exists in the case of the olfactory and taste cells.

Blood-vessels.—There are no blood-vessels in contact with the epithelial cells on the skin and mucous membranes. The epithelium must derive its nourishing particles immediately from the lymph ; and it has already been stated that between the cells in the lower layers of stratified squamous epithelium there are spaces (Fig. 26) that are probably lymph channels. In glands, however, especially in the liver, the blood-vessels come into very near relation to the epithelial cells, doubtless for the purpose of readily permitting of an interchange of material between them.

CHAPTER VIII.

THE CONNECTIVE TISSUES.

The group of connective tissues embraces cartilage, mucous tissue, retiform tissue, ordinary connective tissue, and bone. Their functions are in all cases purely mechanical, and depend on the nature of the periplast, as will be explained in detail. All the connective tissues have so close a genetical relationship, that it is advantageous, as Reichert proposed, to group them together.

Cartilage.

Cartilage is a solid texture composed of cells imbedded in a strong firm periplast that forms a continuous fibrillated or homogeneous matrix. The cells merely discharge the function of secreting the periplast (intercellular substance or matrix) upon whose passive mechanical properties the functions of the tissue depend. Cartilage is of much service in the bodily economy : thus, at an early period of embryonic life, it constitutes a temporary skeleton that eventually gives place to bone in many situations where a less yielding framework becomes necessary, but it remains permanent at the articular ends of the bones, between the ribs and sternum, in the ear, larynx, and other situations where a tissue more yielding than bone, but still of decided firmness, is required. There are three varieties in the human subject—(1) *Hyaline cartilage.* (2) *White fibro-cartilage.* (3) *Yellow fibro-cartilage.*

Hyaline Cartilage.

Hyaline cartilage occurs at the articular ends of the bones, between the ribs and sternum, in the walls of the trachea and bronchi, and in the larynx ; where the thyroid, cricoid, and arytenoid cartilages consist of it. In the mass it is opaque and pearly ; in thin plates, translucent. It is elastic, pliable, and tough, so that it is difficult to break it.

A horizontal slice from the cartilage at the end of the frog's femur, examined in a serous fluid such as aqueous humour, or in a dilute watery solution of alum (1 : 200), shows that the tissue consists of nucleated cells imbedded in a hyaline matrix (Fig. 39).

THE CELLS are more or less rounded, and often somewhat angular. Each cell (*a*) is a mass of finely-granular protoplasm with a well-defined spherical nucleus, and often two or or three nucleoli. The protoplasm entirely fills the cell space, but if water and various other re-agents be added, it shrinks (*e*), and, gathering around the nucleus, leaves a clear space in the periphery of the cell cavity: *proving that protoplasm* is a sponge-like substance with interstices full of fluid. When the protoplasm shrinks from the capsule there is no evidence of a laceration of the protoplasm, as must have occurred, were the capsule a mere hardening or other transformation of the outer part of the protoplasm, as some have imagined. The cells may be stained by various agents, of which *gold-chloride* is perhaps the best. It dyes the cells violet, without causing them to shrink. *Iodine solution* stains the cell substance pale yellow, and reveals the presence of *particles* of glycogen by rendering them brown. *Osmic acid* slightly darkens the general cell substance, and renders *black* any *fatty particles* that may be present.

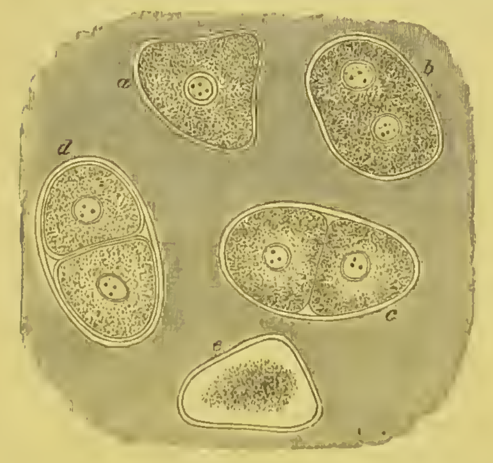

Fig. 39. Articular cartilage from head of frog's femur. Examined in alum solution (1 : 200). *a*, Typical cell with clear capsule; *b*, cell with divided nucleus; *c*, cell with divided nucleus and protoplasm; *d*, two cells within a primary capsule, each with a secondary capsule; *e*, cell with protoplasm shrivelled around the nucleus. × 800. (The protoplasm in *c* is too faint. It ought to have been drawn darker than in the other cells, somewhat like *b* and *c* in Fig. 21.)

The transmission of electrical shocks through a thin plate of living cartilage, *e.g.* the ensiform cartilage of the newt, occasions a sudden shrinking of the cells, such as happens when a white blood-corpuscle is thus excited. By Rollett (*Op.* 38, i. p. 98) the shrinking is ascribed to contraction; but Heidenhain (*Op.* 49, Heft 2, p. 1), who discovered this fact, maintains that as the protoplasm never relaxes and refills the cell-space, the electricity, like water and other re-agents, simply occasions coagulation of the proteids in the protoplasm.

THE MATRIX (*intercellular substance or periplast*) has the appearance of ground glass. It is hyaline, faintly granular, and without special methods of preparation appears homogeneous. It is secreted by the cells, around each one of which the newest part of the matrix constitutes a clear homogeneous *capsule*, at first distinct, but becoming after a time so fused with the surrounding matrix as to be undistinguishable from it. The matrix may be stained of a brown colour by the silver process, and by this means the capsule around each cell is often very clearly defined.

Outside the cell-capsule the matrix appears homogeneous, but is in reality fibrillated, as was first pointed out by Leidy, an American histologist. The fibrillation may become very evident in some pathological states of cartilage, as Redfern was the first to show (*Op.* 7, August 1849). Recently this point has been reinvestigated by Tillmanns (*Op.* 18, x. p. 401; (*Op.* 16, Anat. Abtheil., year 1877, p. 9) and Baber (*Op.* 1, x. p. 113), who show that the matrix consists of fine fibrils held together by a clear homogeneous cement-substance, that may be dissolved or softened by certain re-agents, after which the fibrils become visible. The fibrils may be seen without much difficulty by placing a thin slice of articular cartilage of a frog for three days in a 10 per cent solution of sodium chloride, as Tillmanns recommends. Pressure on the cover-glass is sometimes required to bring them into view. Tillmanns also recommends (*Op. cit.* 16) digestion with trypsin (the proteolytic ferment of the pancreas) as a means of demonstrating them. The tryptic digestion dissolves the cement-substance and leaves the fibrils. The fibrils are clear and homogeneous, and run in branching bundles. In some places they are at a distance from the cells with an intervening homogeneous matrix, in other situations they run in bundles towards the cell-capsules and seem to end abruptly there.

Production of the Matrix.—One point of importance in the histology of cartilage is the clearness with which the production of the periplast by the cells may be traced. The nucleus and then the protoplasm divide into two (Fig. 39, *b c*). The cell capsule does not grow inwards between them, but each protoplast secretes around it a new capsular periplast, that may by very careful illumination be seen within and quite distinct from the capsules previously formed (*d*). The latter after a time becomes indistinguishable from the surrounding periplast, and probably undergoes a molecular transformation into the fibrils and cement-substance already mentioned. Although the growth of the capsule in some way depends on the protoplasm, there is no evidence of any direct transformation of the one into the other; the two—though in apposition—seem to be as structurally distinct as the protoplasm freely moving inside the periplast of the cells of Tradescantia (Fig. 6). Yet in that case as in this the periplast is produced by the protoplasm.

CHEMISTRY OF CARTILAGE.—The matrix yields chondrin by prolonged boiling. Chondrin is an albuminoid matter allied to gelatine (p. 37), the substance obtained by boiling white fibrous tissue. As chondrin, unlike the cartilage matrix, is readily soluble in hot water, it is supposed to be derived from a hypothetical substance termed chondrogen. That chondrogen is derived from proteids under the influence of the cartilage cells cannot be doubted, but there is no evidence of any actual transformation of the peripheral part of the protoplasm into the matrix as some have supposed.

The general composition of hyaline cartilage (articular) is water 73·59, organic matter 24·87, inorganic solids 1·54 per cent.

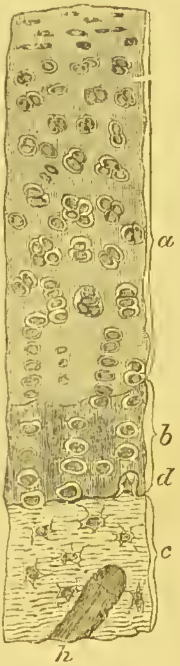

Fig. 40. Vertical section, head of radius of full-grown cat. *a*, Articular cartilage; *b*, zone of calcified cartilage; *c*, bone; *d*, cartilage cell passing into a bone-corpuscle: *h*, Haversian canal. × 300 (*reduced*).

IN A VERTICAL SECTION OF ARTICULAR CARTILAGE (Fig. 40) the cells are flattened near the articular surface, where the cartilage is gradually worn away by the movement of the joint. Cell-proliferation occurs throughout the whole substance of the cartilage; hence the irregular grouping of the cells. But it probably takes place most rapidly near to the bone, where the cells are in rows, owing to the cell-cleavage in this situation always taking place at right angles to the axis of each row.

Near to the bone (*b*) there is a zone where the matrix of the cartilage is very evidently fibrillated and impregnated with calcareous matter.

Costal Cartilage from an adult shows the fibrillation of the matrix far more distinctly (Fig. 41 *f*). Here and there throughout the cartilage the cells proliferate and form irregular groups or rows (*c*), in the neighbourhood of which fibrillation of the matrix becomes very evident. The fibrils are of a yellowish colour, run parallel one with another, and unlike those of white fibrous tissue do not swell up in acetic acid. The fibrils appear to be calcified. The relation between these calcified fibrils and the original and far less evident fibrils of the matrix is not as yet determined, but it is perfectly clear that the cartilage periplast may become the seat of important structural and chemical changes.

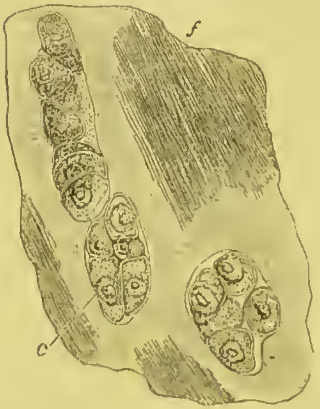

Fig. 41. Costal cartilage of adult. c, Cells; *f*, fibrillated matrix. × 300. (Drawn after staining with picric acid, which reveals the capsules of the cells clearly.)

As cartilage grows old, fatty transformation of the cells and calcification of the matrix are very apt to occur. Both may be seen in the costal, laryngeal, and tracheal cartilages of old persons. Fatty particles appear amidst the protoplasm, and may become so numerous that they almost entirely take its place (fatty degeneration). When the matrix becomes calcified, the mineral particles may appear irregularly scattered around the cells in the matrix, which otherwise appears unchanged, or the matrix may become obviously fibrillated.

Development.—Cartilage is developed from the mesoblast. Nucleated protoplasts secrete around them a hyaline capsule. The capsules of neighbouring cells are, as it were, pressed together to form the matrix, which is at first in small amount relatively to the cells. This relatively small production of the periplast is a permanent characteristic of the so-called *parenchymatous* or *cellular* cartilage of the ear of the mouse, bat, and some other animals; but usually this condition is transient. The cells produce a relatively large quantity of matrix, and ordinary hyaline cartilage is the result. The growth of the matrix has already been described.

Perichondrium.—Excepting the case of articular cartilage, all the other hyaline cartilages are enveloped in a vascular fibrous membrane—the perichondrium. It chiefly consists of white fibrous tissue, and it is instructive to observe the gradual transition between the hyaline, apparently homogeneous, periplast of the cartilage, and the obviously fibrillated periplast of the fibrous tissue, and between the cells of cartilage and those of the fibrous tissue. There is no abrupt line of demarcation between the two tissues. But the fibrous tissue periplast decidedly differs, chemically, from that of the cartilage, for while acetic acid causes the former to swell and become very transparent, it does not affect the latter. Moreover, boiling extracts gelatin from the former but chondrin from the latter,—both albuminoid substances however.

As already stated, the surface of articular cartilage that is exposed to friction is bare. This, however, is true only after the joint has been used, for previous to that time, as shown by Henle, the free surface is covered by a layer of endothelium continued from the synovial membrane. At all ages, however, the peripheral part of the articular surface that is not exposed to friction is covered by a very vascular layer of the synovial membrane.

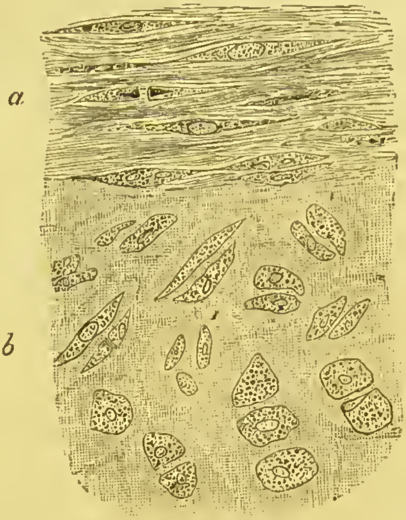

Fig. 42. The peripheral part of a transverse section of a tracheal ring. *a*, perichondrium; *b*, cartilage. × 600.

VESSELS AND NERVES.—Articular cartilage, being non-vascular, depends for its nutrient supply on the blood-vessels of adjacent bone and synovial membrane. Thick pieces of cartilage, such as those of the ribs, have vascular canals containing blood-vessels and connective tissue that penetrate from the perichondrium. These vascular canals, however, are not found in the embryonic state, and only appear as a preliminary to ossification (Ranvier, *Op.* 39, p. 290).

As no capillaries at any time penetrate the general cartilage-matrix, it must be sufficiently porous to allow of the penetration of lymph from the neighbouring capillaries; and proof of this porosity is furnished by the readiness with which a staining agent diffuses into the tissue. Cartilage, probably, does not require a very abundant supply of pabulum, for its metabolism is doubtless tardy, because it is a tissue, where only a slow growth occurs, and thus very different from a muscle, where energy is rapidly evolved; or a gland, where substances for secretion are quickly required, and where, therefore, the vessels are brought, it may be, into actual contact with each cell. Neither lymphatics nor nerves have been found in cartilage, and it is devoid of sensibility.

IRRITATION OF CARTILAGE.—Goodsir (*Op.* 50, ii. p. 408) first pointed out that when articular cartilage ulcerates, its cells proliferate, and a brood of them fills each cell-space which thus becomes enlarged. At the joint the cell-capsules are opened by absorption, and the young cells are discharged. Redfern (*Op.* 7, year 1849) confirmed Goodsir's observation, and further showed (*Op. cit.*, year 1850) that when articular cartilage is irritated by the introduction of a foreign body, such as a seton, cell multiplication occurs. When the irritation is not excessive, each young cell produces a cartilage capsule. But with excessive irritation the vital action of the protoplasts becomes seriously altered; they do nothing but multiply, and cease to produce a periplast; and instead of an increased *production* of cartilage, its *destruction* in the manner described by Goodsir is the final event. The degenerated descendants of the irritated cartilage-cells closely resemble pus-corpuscles. Upon Goodsir and Redfern's observations Virchow founded his *Cellular Pathology* (*Op.* 32), and their great and fundamental importance consists in this, that they afford a clear and unequivocal demonstration of the germinal activity inducible in cells by appropriate irritation. A mild excitement increases germinal activity without altering the physiological characteristics of the particular cells concerned, but powerful irritation profoundly alters them.

In many situations pus corpuscles, to some extent at all events, are certainly emigrated white blood-corpuscles; but in articular cartilage we have a texture whose matrix prevents the entrance of blood corpuscles; and therefore, although it may be doubted that the cell-broods of the irritated cartilage are identical with pus cells, they are, at all events, not unlike them, and are formed *in situ*.

White Fibro-Cartilage.

The intervertebral discs, sacro-iliac synchondrosis, symphysis pubis, inter-articular cartilages, glenoid and cotyloid ligaments, and the cartilages that deepen the grooves for tendons—all consist of white fibro-cartilage. It consists of a matrix of very fine colourless fibrils (Fig. 43 *d*) similar to those of white fibrous tissue (Fig. 51), surrounding cells resembling those of hyaline cartilage. Each cell is a nucleated protoplast with a clear homogeneous capsule. The cell may be single (*a*), but many instances of proliferation may be found where a single capsule encloses two cells (*b*, *c*). There is, therefore, in this tissue, as in hyaline cartilage, a twofold periplast — the clear homogeneous cell capsule and the fibrillated substance. But here, unlike hyaline cartilage, the fibrils are obvious without special preparation, owing to the small amount of cement substance. Whether or not the fibrillated matrix is here, as in hyaline cartilage, a transformation of the cell-capsule, remains to be shown. Chemically, this tissue is more closely allied to white fibrous tissue than to cartilage, inasmuch as, on boiling, it yields gelatine.

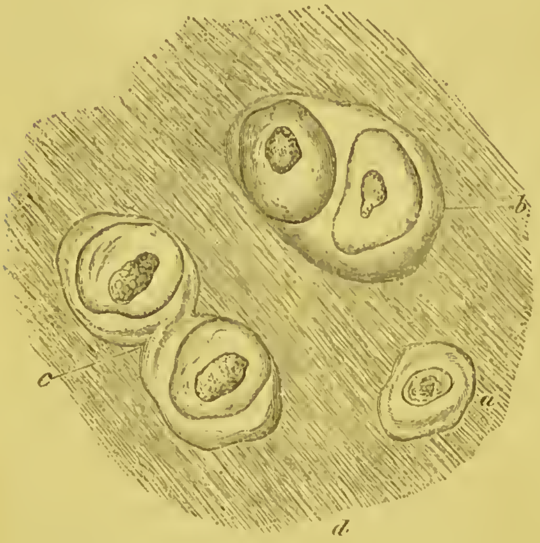

Fig. 43. White fibro-cartilage from periphery of intervertebral disc of ox. *a*, *b*, *c*, Cells; *d*, matrix. × 860.

In the centre of the intervertebral disc the cartilage has no fibrillated matrix. Many of the cells are similar to those of white fibro-cartilage, but often a single capsule encloses a brood of young cells. This central part of the disc is probably directly descended from the cells of the chorda dorsalis of the embryo.

Yellow Fibro-Cartilage.

Yellow fibro-cartilage (reticular, spongy, or elastic cartilage) occurs in the epiglottis, corniculæ laryngis, in the outer ear, and in the Eustachian tube. It is more flexible than hyaline cartilage, has a yellow colour, and its cut surface has a spongy appearance.

The structure of this tissue may be best comprehended by tracing the transition between it and hyaline cartilage, as it may be found at the root of the epiglottis, or at the apex of the arytenoid, where its hyaline cartilage gradually merges into the elastic cartilage of the cornicula laryngis. A network of fibres identical with those of elastic tissue (Fig. 49) appears in the hyaline matrix (Fig. 44, *h*). These increase in number, until they almost entirely replace the hyaline matrix, and thus the hyaline becomes, as it were, yellow fibro-cartilage (*e*). Cartilage cells are found amidst the feltwork of elastic fibres, and immediately round them there is usually a layer of hyaline matrix in which elastic fibres have not yet appeared. In the epiglottis, the elastic reticulum is so close (Fig. 45, *a*) that it resembles a sponge rather than a feltwork of fibres, although here and there the meshwork is so open that the bridges appear as fibres. Hyaline matrix (*c*), not yet differentiated into the elastic reticulum, surrounds the cells (*b*), and to some extent fills the interstices of the sponge-like reticulum.

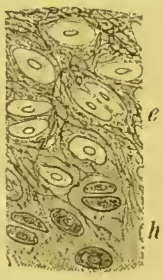

Fig. 44. Transition between hyaline (*h*) and elastic cartilage (*e*). From lower part of epiglottis of sheep. × 30

The transition of hyaline into elastic cartilage, above traced, is a permanent picture of the embryonic development of the latter. In the embryo it is preceded by hyaline cartilage, in whose matrix the elastic material makes its appearance. Some maintain that the elastic substance is a direct transformation of the protoplasm of the cells, but of this we have failed to find the least evidence. It may be clearly seen, in the case of the elastic fibres at all events, that, as H. Müller (*Op.* 51, x. p. 132) stated, they are produced within the matrix often at a distance from the cells, apparently by the coalescence of fine granules of elastic material that probably result from a metabolism of chondrogen.

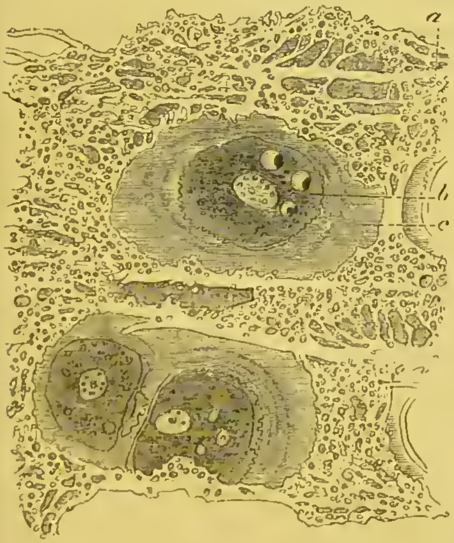

Fig. 45. Spongy cartilage from epiglottis of sheep. *b*, Cell; *c*, hyaline matrix around it; *a*, elastic network. × 800. (Hertwig, *Op.* 18, ix. p. 80.)

Elastic tissue consists of elastin, a substance that resembles chondrin—only in its albuminoid composition. Unlike chondrin and gelatin, it is quite insoluble in hot water; and, unlike gelatigenous tissue, it is unaffected by acetic acid. But though exceedingly insoluble, the elastic material may be dissolved by prolonged maceration in a strong solution of caustic potash, in which it breaks down into granules that dissolve on the addition of water. Elastic cartilage when boiled yields a small quantity of chondrin.

MUCOUS TISSUE.

Mucous, or jelly-like connective tissue, is the permanent connective tissue of the cephalopoda and many other invertebrates. In the human embryo it is the predecessor of other forms of connective tissue, viz. retiform and ordinary connective tissue. In the adult it occurs only in the vitreous humour, but in pathological states it sometimes reappears and constitutes myxomatous tumours.

The typical structure of this tissue is found in cephalopods, in the early embryo, and in the *outer* part of the vitreous humour. It consists of cells in a clear, homogeneous, jelly-like matrix or periplast (Fig. 46, *m*). The cells are nucleated protoplasts of two sorts—1. *Stationary cells* with delicate processes anastomosing with those of their neighbours (*c*). These are the *connective tissue corpuscles proper.* 2. *Amœboid or wandering cells*, more or less rounded in shape, and apparently identical with white blood-corpuscles. The branched corpuscles are generally the more numerous of the two, but throughout the greater part of the vitreous humour of the adult they are absent, and only the amœboid cells are found.

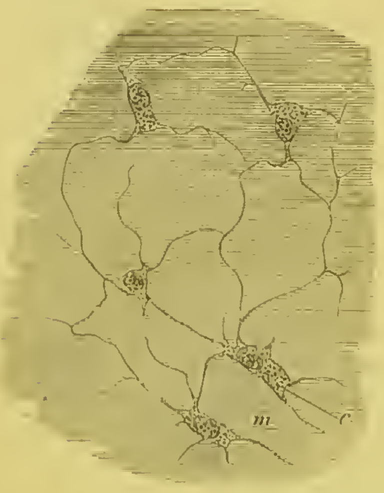

Fig. 46. Mucous tissue from the periphery of the vitreous humour. *c*, Corpuscles. *m*, jelly-like matrix. × 300. *The lines in the matrix are merely for shading.*

In the other parts of the body, where the preliminary mucous tissue gives place to tissues that are permanent, two different transformations occur. The matrix may disappear, while the processes of the corpuscles become thicker and stronger, and constitute *retiform* tissue (Fig. 47). Or the fibrils of white fibrous tissue may appear in the matrix, altogether independent of the cells (just as fibrils make their appearance in the hyaline matrix of cartilage, p. 41), and the tissue thus tend towards ordinary connective tissue. This is its condition in the so-called Wharton's jelly of the umbilical cord. The continuation of this transformation that occurs when the tissue gives rise to ordinary connective or fibrous tissue will be described later.

The cartilage of cephalopods closely resembles mucous tissue in structure. Its cells form a network, but the jelly-like matrix is replaced by the firm matrix of cartilage. *This cartilage, with ramified cells, sometimes appears with mucous tissue in myxomatous tumours.*

Mucous tissue yields mucin and albumin. The latter is probably derived from the lymph with which the tissue is bathed, but the mucin is doubtless produced by the agency of the cells.

RETIFORM TISSUE.

Retiform or adenoid (His) connective tissue occurs in the spleen and lymph glands, in the alimentary mucous membrane, and especially in the intestine, and in the bronchial mucous membrane. It consists of ramified connective tissue corpuscles, whose branches form an anastomosing reticulum (Fig. 47). The intervening spaces, which in the mucous stage of this tissue were filled with a jelly-like matrix, now contain lymph, and it may be lymph-corpuscles. The protoplasm of the corpuscles have become transformed into a periplast, consisting of a firm and tolerably resistent material. The nuclei may remain, but from many corpuscles they disappear. This tissue may therefore be regarded as mucous tissue, whose periplast has given place to cavities filled with lymph and its corpuscles, and whose cells have been transformed into a new periplast that forms a fibrous reticulum. In this instance the periplast appears to be really a transformation of the protoplasm.

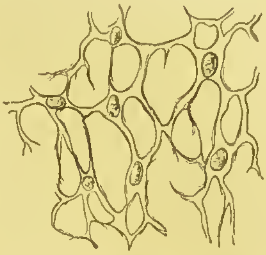

Fig. 47. Retiform tissue from a lymph gland. X 300.

ORDINARY CONNECTIVE TISSUE.

Ordinary connective tissue binds the bones one to another, and to their muscles; it forms sheaths and capsules for cartilage, bone, muscle, and various organs, such as the eye, liver, spleen, etc.; and serves as a connective substance throughout the body generally. In the skin and many other parts it is arranged in the form of an open network; while in tendon, ligament, and aponeurosis it is arranged in a compact form. It consists of nucleated protoplasts, with a periplast that is for the most part fibrous: the fibres being of two sorts—the white or gelatigenous, and the yellow or elastic. Sometimes, however, the periplast is in the form of a membrane, as is the case in the elastic membrane of blood-vessels. It is convenient to study separately—1, *The structural elements of ordinary connective tissue,* viz. (*a*) an elastic element, (*b*) a gelatigenous element, (*c*) cellular elements; 2, *Their arrangements.*

1. *Elements of Ordinary Connective Tissue.*

a. THE ELASTIC ELEMENT OF ORDINARY CONNECTIVE TISSUE (ELASTIC TISSUE) is of much service in various parts of the economy because of its extensibility and elasticity. Thus, in the lungs it readily allows of their distension during inspiration; and by its power of recoil it is an important agent in the production of the act of expiration. It gives to arteries and veins the properties of elastic as contrasted with rigid tubes. By giving elasticity to the vocal cords it is of service in the production of voice. It also gives elasticity to the skin and various other parts. It is composed of elastin, an albuminoid substance already referred to (p. 37), but whose insolubility in acetic acid may be again specially mentioned. Elastic tissue is mostly *fibrous,* but in some situations *membranous.* Both varieties usually occur amidst or in contact with white fibrous tissue.

The fibrous variety of elastic tissue (yellow or elastic fibrous tissue) occurs in the ligamentum nuchæ and ligamenta subflava, in the true vocal cords, stylohyoid ligament—the thyrohyoid and cricothyroid membranes. It is also found in the lung, skin, and generally wherever white fibrous tissue occurs, some elastic tissue is intermingled with it.

Elastic fibres are of a pale yellow colour. In the vertebral ligaments they are coarse—being about 8 μ ($\frac{1}{3200}$ inch) in diameter (Fig. 48). In other situations they are much finer (about 1 μ, or $\frac{1}{24000}$ inch). They are of indefinite length, are branched, often curl up at the ends, refract the light strongly, and have therefore a sharply defined outline. They are unaffected by acetic acid. Sometimes there are rounded holes or fissures in the fibres, but usually they are homogeneous and solid. They have no nuclei.

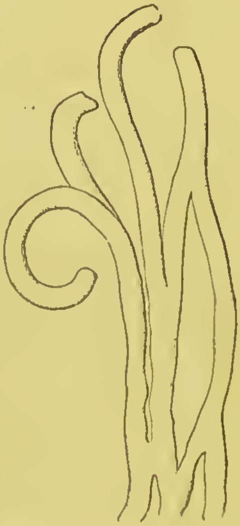

Fig. 48. Coarse elastic fibrous tissue from ligamentum nuchæ of ox. × 250.

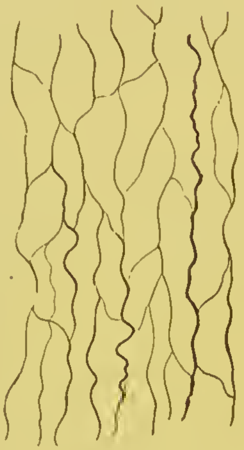

Fig. 49. Fine elastic fibrous tissue from peritoneum of child. × 350 (Kölliker.)

The membranous variety of elastic tissue occurs principally in arteries and veins. The membrane may be of uniform extension, or it may be pierced with holes (fenestrated) of various sizes (Fig. 50), sometimes indeed so large that the membrane becomes virtually a network of elastic fibres.

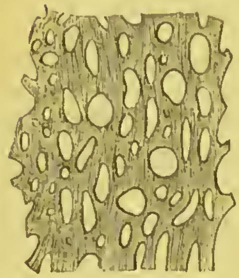

Fig. 50. Elastic membrane from carotid artery of horse. × 350. (Kölliker.)

b. The Gelatigenous Element of Ordinary Connective Tissue is so called because on boiling it yields gelatine. It is nearly always in the form of *fibrils*, which are usually gathered into bundles—the *gelatigenous or white fibres* (white fibrous tissue). In some situations, however, *e.g.* in the delicate sheath of Schwann that envelopes nerve fibres, it constitutes a homogeneous *membrane.* The white or gelatigenous element is usually much more abundant than the elastic element in ordinary connective tissue, except in the elastic ligaments already mentioned, where the elastic element greatly preponderates. The gelatigenous element is almost devoid of extensibility, and is therefore fitted to constitute tendons, aponeuroses, and those ligaments in which stretching is undesirable. In these cases the elastic tissue element is almost entirely absent.

The difference between the elastic and white connective tissue fibres, as regards extensibility and elasticity, may be readily apprehended by comparing a strip of ligamentum nuchæ with a tendon. The ligament is very *extensible*, and when relieved from the stretching force recoils to its original length. Expressed in the precise terms of the physicist, the elasticity of the ligament is *small in amount* but *perfect in quality*. On the other hand, the tendon, though extremely supple and pliable, is *almost inextensible*, and when it does yield to a powerful force it fails to regain its original length when the stretching is discontinued. It has therefore a *large amount* of elasticity, but of an *imperfect quality*. It thus resembles a flaxen cord, while the ligament is like an india-rubber band. For convenience, the term elastic is in ordinary phraseology commonly applied to those bodies whose elasticity is *perfect in quality* though *small in amount*.

The structure of white connective tissue fibres may be readily studied in the deep layer of the skin. Each fibre is a round or flattened filament of indefinite length (Fig. 51, *b*), and usually about 8 μ ($\frac{1}{3200}$ inch) in breadth. It is colourless, transparent, and, owing to its feeble refractive power, is bounded by a faint outline: in this respect, therefore, strongly contrasting with elastic fibres (*a*). When unstretched it assumes a wavy form. The fibre may appear homogeneous, but by teasing with needles it readily splits into a bundle of fine fibrils. They resemble threads of spun glass, are homogeneous, unbranched, and only about half a *micro* ($\frac{1}{50000}$ inch) in diameter. The circumstance that cleavage of the fibre into fibrils is very readily effected after maceration in lime or baryta water, in a ten per cent solution of sodium chloride (compare hyaline cartilage, p. 77), or in solutions of potassium bichromate or permanganate, has led to the belief that the fibrils are united by an interstitial cementing substance. The matter dissolved by the lime-water agrees in its reactions with mucin (Rollett, *Op.* 38, i. 72). The fibres are sometimes encircled by fibrous or membranous rings (*b*). These are very common in the fibrous tissue of the subarachnoid space, where the fibres are often encircled not by rings but by networks (Key and Retzius, *Op.* 52, vol. i. Plate 14, Fig. 9). These rings and networks resemble elastic tissue inasmuch as they are not affected by acetic acid, but they cannot be regarded as identical; for, as Ranvier (*Op.* 39, p. 338) has shown, they, like the white fibres, are coloured red by picrocarmine, while the elastic fibres remain colourless. When dilute acetic acid is added to the white fibres, their fibrillar structure disappears, they become exceedingly transparent, and swell. If constricting rings are present (*b′*) the fibre swells between

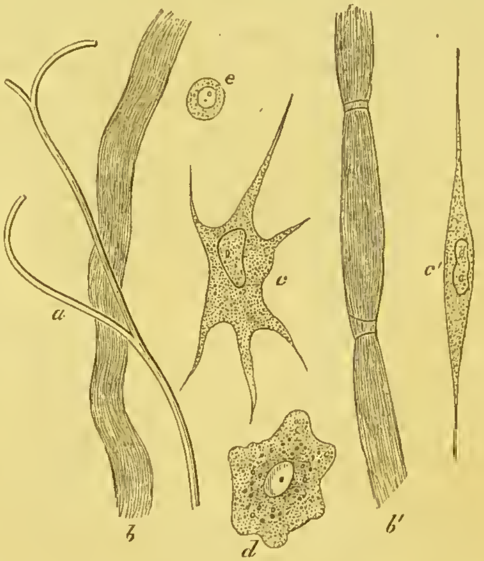

Fig. 51. Elements of ordinary connective tissue. *a*, Elastic fibre; *b b′*, white fibres; *c d*, connective tissue cells; *c′*, profile view of the same; *e*, wandering cell. (From subcutaneous tissue of young rabbit.) × 350.

them, and assumes a beaded appearance. The white fibres consist of a gelatigenous substance termed collagen, which by boiling is converted into gelatine, whose properties have been already alluded to (p. 37).

c. THE CELLULAR ELEMENTS OF ORDINARY CONNECTIVE TISSUE are—1. *The ordinary or finely-granular cells.* 2. *The wandering cells.* 3. *The coarsely-granular cells.*

1. *The ordinary connective tissue corpuscles are fixed*, and usually somewhat flattened cells. The nucleus is usually more or less oval, and mostly surrounded by some undifferentiated protoplasm. The whole corpuscle in its young state is simply a nucleated protoplast; but in the fully-formed condition, the outer part of the protoplasm is sometimes transformed into a thin transparent homogeneous plate, with or without fine processes of a similar nature. The cell may be a simple epithelioid plate without marginal processes, but usually its margins are prolonged into delicate processes (Fig. 51, *c*). The corpuscle may occur singly, or its processes may anastomose with those of neighbouring cells, and form a network, as may be well seen in the cornea (Fig, 52). Viewed edgewise, the flattened cell resembles a spindle (Fig. 51, *c'*), the central bulging being due to the nucleus. But sometimes the branched connective tissue corpuscle is a *compound plate;* either a series—from four to six—projecting from a central nucleated mass, like the spokes of a wheel, or a principal plate containing the nucleus and giving off at various angles a few smaller plates from its surface; all the plates usually ending in fine processes (Waldeyer, *Op.* 18, xi. 176). The cells are motionless, and they are usually colourless, but in the choroid coat of the eye (Fig 53) they are loaded with dark brown granules of melanin (p.). The contractile pigment cells of the frog will be afterwards alluded to. The appearance of fat within the contive tissue cells will also be specially described.

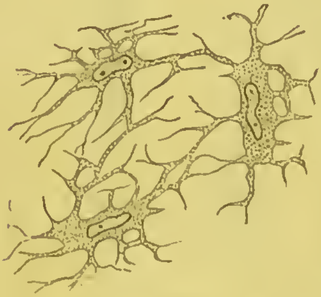
Fig. 52. Branched connective tissue cells of cornea of frog. × 300.

2. *The wandering or amœboid connective tissue corpuscles* (or leucocytes) are nucleated cells resembling lymph or white blood-corpuscles (Fig. 51, *e*). They are chiefly found in loose connective tissue, and migrate from one place to another through its lymph spaces. Some of them certainly are, and it may be that *all* of them are, white blood-corpuscles that have emigrated from the vessels. Probably some of them find their way into the lymphatics, and thus leave the tissue; but in the tadpole's tail they shoot out processes, and become branched connective tissue corpuscles (Fig. 14). The wandering cells not so numerous as the ordinary fixed connective tissue corpuscles.

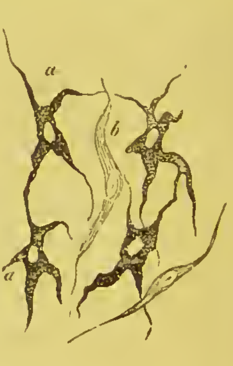

Fig. 53. Connective tissue corpuscles from stroma of human choroid. *a*, Cells with pigment; *b*, Colourless cells. × 350. (Kölliker.)

3. *The coarsely-granular corpuscles* are, in most situations, few in number compared

with the other cells of connective tissue. They (Fig. 51, *d*) consist of a nucleated mass of coarsely-granular protoplasm, three or four times the size of the wandering cells; usually, however, there is no amœboid movement; but in the delicate intermuscular fascia of the frog's leg they may be seen to slowly change their form (Kühne). They have no distinct processes, and are usually more or less rounded in shape. In ordinary areolar tissue they may be found in small number, usually in groups around the blood-vessels. Fat sometimes appears within them, and they become transformed into fat cells. Waldeyer (*Op.* 18, xi. p. 190) proposes to designate these cells the "embryonal cells of connective tissue," or "plasma cells;" but both terms are objectionable, because, as he himself points out, they may be developed from ordinary connective tissue cells; and certainly the term "plasma" is too ambiguous. Boll (*Op.* 18, vii. p. 322) pointed out the similarity between these cells and the so-called "interstitial" cells of the testis; and Waldeyer (*Op. cit.*) refers to the same category other peculiar groups of cells, whose histological significance has hitherto been obscure — viz. the cells of the coccygeal body (Fig. 54), corpus luteum, suprarenal capsule, and the serotinal cells of the placenta. Waldeyer states that in all these situations the cells are developed from ordinary connective tissue corpuscles, and always envelope the blood-vessels (Fig. 54). The functions, if any, of the cells in these organs are unknown.

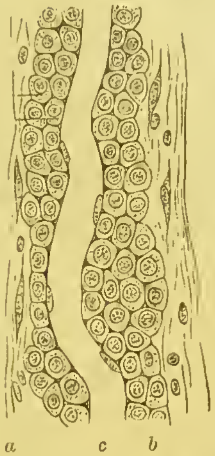

Fig. 54. Part of the coccygeal body.[1] *c*, Capillary; *a*, connective tissue sheath; *b*, coarsely-granular cells. (Eberth.)

2. *Arrangement of the Elements of ordinary Connective Tissue.*

The fibres of ordinary connective tissue may be arranged loosely, as in areolar tissue; or compactly, as in tendon, aponeurosis, cornea, etc.

a. THE AREOLAR FORM OF FIBROUS TISSUE.—The *areolar* is the most common form of connective tissue, and occurs in the deep layer of the skin, and in many other parts. The fibres are arranged in an irregular open network, the white being much more numerous than the elastic fibres. Sometimes an elastic fibre appears to lie within a white fibre (Key and Retzius, *Op.* 52, i. plate 14, fig. 12), but this is rare. Almost always they run irregularly in the spaces between the white fibres. The irregular spaces between the fibres are filled with lymph (lymph spaces), and by a free intercommunication allow of a ready percolation of the lymph from one part to another. The effect of this is seen in dropsy, where the lymph drains through the areolar tissue to the most dependent part; and also in cutaneous emphysema, when the lymph spaces become distended with air, which freely moves from one part to another. Normally, the lymph spaces are in a collapsed state. The amœboid cells wander about in them. The ordinary connective tissue corpuscles are also within them, but not lying loose as they appear after dislocation by artificial means, but in contact with and *clasping* the white fibres as shown by Ranvier (*Op.* 39, p. 342). They may clasp and partly or completely surround a single fibre, or a bundle of fibres. In some situations, *e.g.* in the omentum and in the subarachnoid space, they are epithelioid in shape, and by the apposition of their margins form a complete envelope to a single fibre, as seen in the tissue of the subarachnoid space (Key and Retzius, *Op. cit.*), or to bundles of fibres, as occurs in the omentum (Fig. 55), but in ordinary areolar tissue the cells are detached, and as simple plates with processes clasp the fibres, or as compound plates are in contact with a number of fibres. This arrangement, however, is most common in compact fibrous tissue, where the fibres are, as it were, pressed against the cells. As the lymph spaces between the fibres contain the cells, they are sometimes spoken of as cell-spaces. The coarsely-granular cells occur here and there in areolar tissue, sometimes singly, but mostly in groups around blood-vessels.

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[1] A description of the coccygeal body by Eberth may be found in *Op.* 38, i. p. 295.

The omentum consists of areolar tissue, and is of special interest on account of its cells. In a full-grown animal the membrane is cribriform (Fig. 55), and the spaces are filled with lymph contained within the cavity of the peritoneum, of which the omentum is an extension. Its trabeculæ are bundles of connective tissue fibres, mostly white, and are enveloped in endothelial plates, whose outlines may be rendered evident by the silver process. The larger plates are nucleated. Amidst the fibrous bundles there lie ordinary branched connective tissue corpuscles (*c*), that are spindle-shaped when seen in profile, but are in reality lamelliform.

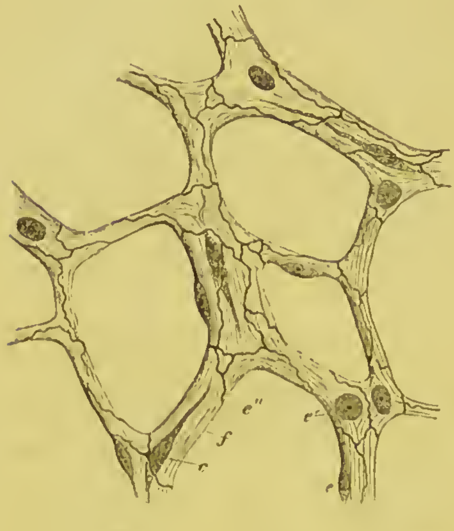

Fig. 55. Omentum of cat, drawn after staining with silver nitrate and logwood. *f*, Trabeculæ of fibrous tissue; *c*, ordinary connective tissue corpuscle; *c*, profile; *c'*, superficial view of nuclei of endothelial cells; *c''*, silvered outlines of the cells. × 300.

A serous membrane everywhere consists of fibrous connective tissue, covered with a layer of endothelial cells. But these, as their development shows, are only modified connective tissue corpuscles. The lymph spaces in ordinary areolar tissue are serous cavities in miniature; the connective tissue corpuscles, though clasping the fibres, not however, in general, forming a continuous covering.

b. THE COMPACT FORM OF FIBROUS TISSUE.—*Tendon* chiefly consists of white fibrous tissue, with some elastic tissue intermingled. The fibrous bundles mostly run longitudinally, closely packed together with small intervening cell spaces. After the action of a ten per cent solution of NaCl, the fibrils and cells may be isolated by teasing with needles. The cells are mostly fusiform, but in reality all of them are flat; if unstained they are difficult to detect except when seen edgewise, when they appear fusiform owing to the bulging nucleus.

In a vertical section of tendon hardened in alcohol or picric acid, and stained with carmine, rows of spindle-shaped cells are seen placed longitudinally (A, Fig. 57). The arrangement of the cells may be, however, most easily studied in the fine tendons in the tail of a rat (Ranvier). The tendons are stained with gold chloride, and rendered transparent by acetic acid. The gold salt stains the cells of a violet colour, whilst the acetic acid, in addition to facilitating the reduction of the gold salt, renders the fibres so transparent that the stained cells can be seen (B). On separating the fibres with needles, the cells are seen to be somewhat quadrangular plates (a'), *clasping the fibrous bundles* (as Grünhagen first indicated, *Op.* 18, ix. p. 282), and extending about half-way round them (Boll). The margins of the cells are said by Grünhagen to be continued into very slender filamentous processes. The cells are mostly in pairs, the nuclei of each pair being close to the contiguous borders of the cells, as if the pair had resulted from cleavage. A bright stripe, termed by Boll (*Op.* 18, vii. p. 276) the "elastic stripe," from its resemblance to an elastic fibre, may sometimes be seen running lengthwise in a row of cells (a) ; sometimes there is more than one stripe. According to Ranvier (*Op.* 39, p. 352), Boll's stripes are ridges due to creases in the cells. Externally the tendon is enveloped by a layer of endothelium (C).

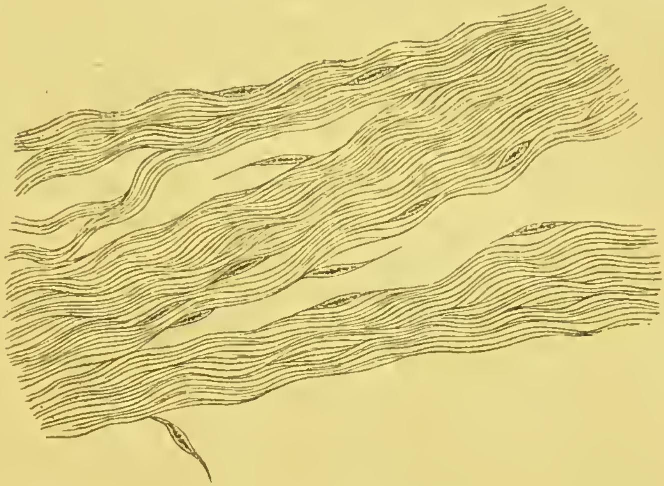

Fig. 56. Human tendon teased with needles, showing fibrils and cells. (Rollett.)

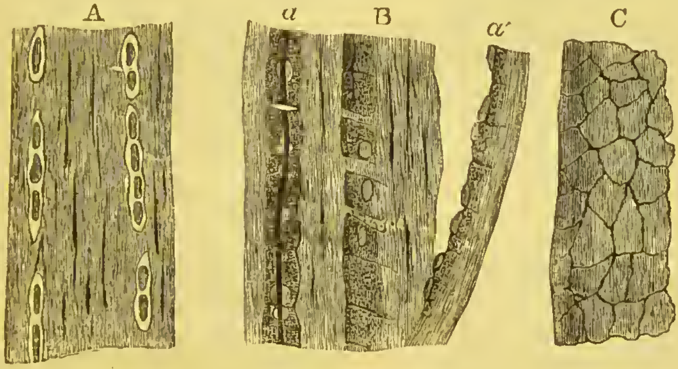

Fig. 57. A, Vertical section of tendon of rabbit, hardened in chromic acid and examined in glycerin. B, Tendon from tail of rat stained with gold chloride. a, Row of cells showing stripe ; a', a fibrous bundle isolated by teasing, showing the cells clasping the bundle. C, Endothelial covering of tendon silvered. × 300.

In a transverse section of tendon (A, Fig. 58), the longitudinal bundles (*b*) are seen to be enclosed in a fibrous sheath (*a*), that sends in branching trabeculæ (*t*), which divide the tendon into a number of compartments each filled with the longitudinal bundles. These may be termed the secondary longitudinal bundles. They in turn consist of primary bundles of fibres, more or less rounded and pressed together, with branching interspaces (*b*), *some* of which contain the tendon cells (B, Fig. 58, *c*), while others appear to contain nothing but lymph.

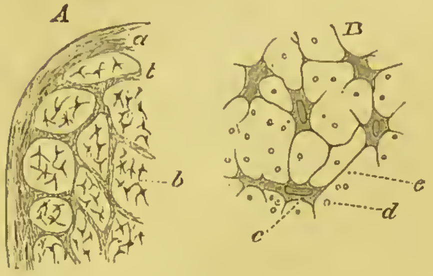

Fig. 58. Transverse section of sheep's tendon. A, × 50. *a*, Fibrous sheath; *t*, trabeculæ; *b*, longitudinal bundles, with branching cell spaces. B, × 300. *c*, Cell; *e*, divided longitudinal bundle; *d*, elastic fibres.

Waldeyer (*Op.* 18, xi. 176) maintains that the usual form of the tendon cell is that of a compound plate, with one principal plate holding the nucleus, and small secondary plates attached to this at various angles, and extending between the fibres. The appearances of a transverse section favour this idea, but one must guard against the fallacious appearance due to the branching lymph space in which the cells lie.

The central tendon of the diaphragm is another example of compact fibrous tissue in which the relation of the cells to the fibrous bundles and to the cell spaces may be conveniently studied. If the endothelium covering the membrane be brushed away, and the subjacent tissue silvered, the fibres (Fig. 59, *f*) and interstitial cement-substance are darkened, while the cell spaces remain clear, with the connective tissue corpuscles

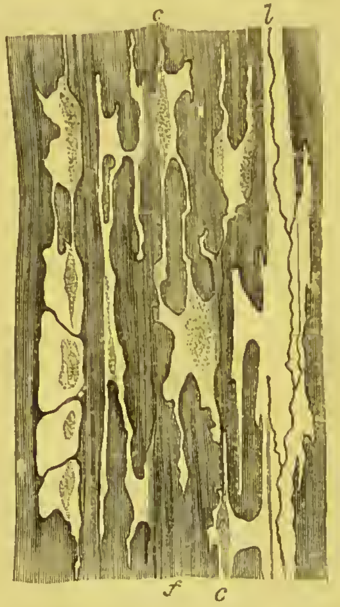

Fig. 59. Central tendon of diaphragm of rabbit silvered after removal of serous covering. *f*, Fibres; *c*, cell spaces with corpuscles; *l*, lymphatic, with silvered outlines of its endothelial wall. × 300.

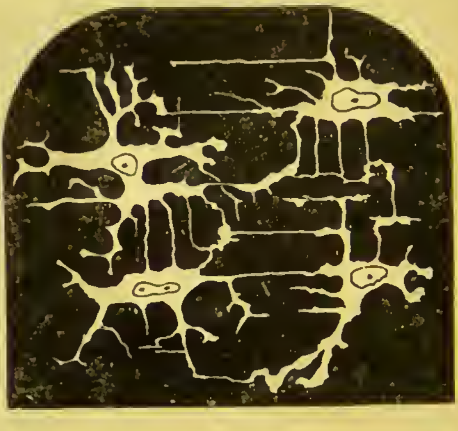

Fig. 60. Superficial view of cornea of frog, silvered after removal of anterior epithelium. The cell spaces and cell nuclei are seen in the darkened fibrous matrix. × 300.

(*c*) within them slightly darkened by the silver. The cell spaces are sometimes quadrangular, but usually they are irregular and branched, anastomosing one with another, and also opening into the lymph capillaries (*l*), so that the lymph can readily percolate through the lymph spaces and flow away by the lymphatics. The cells are flattened, and, after treatment with silver at any rate, rarely fill the whole cell-space.

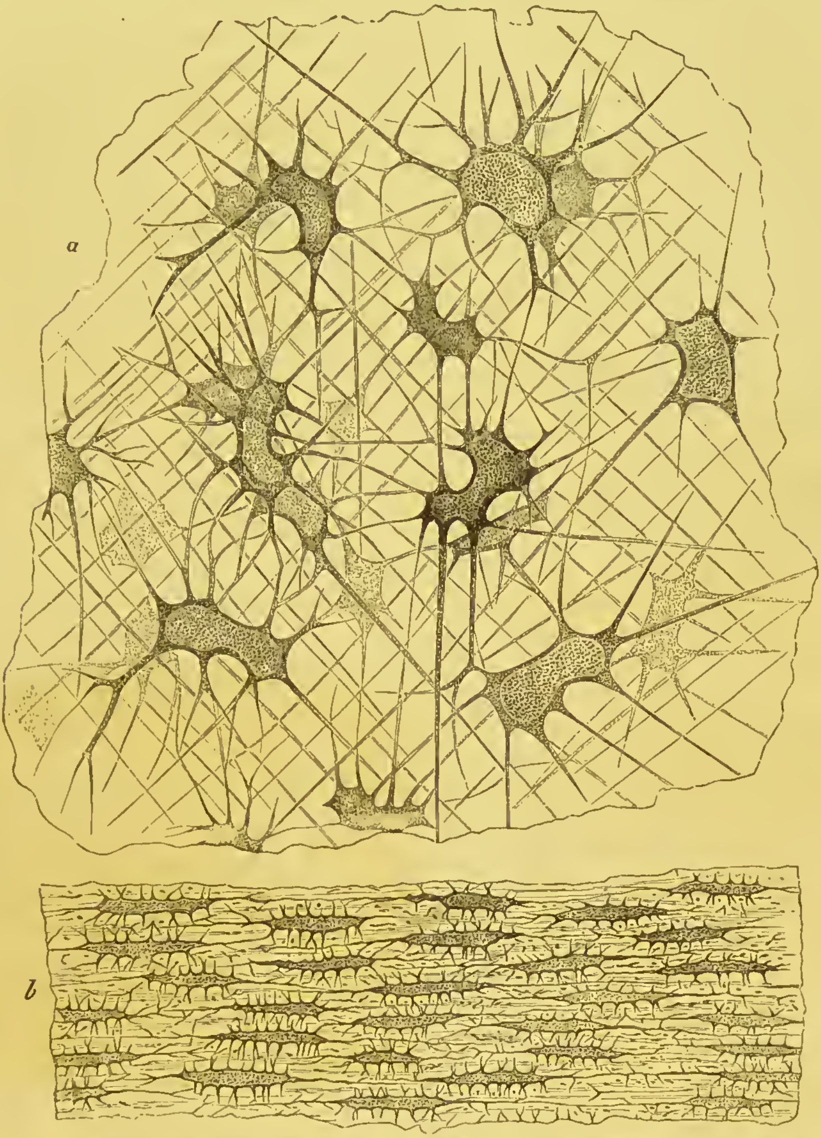

Fig. 61. Fixed corneal corpuscles of frog after staining with gold chloride. *a*, Seen from the surface; *b*, seen in vertical section at right angles to the surface. (Rollett.)

The cornea consists of compact fibrous tissue, and has points of special interest. The fibres resemble those of white fibrous tissue, but instead of being pearly and opaque in mass they are perfectly transparent. They differ also in chemical composition, for on boiling they yield chondrin instead of gelatin. The fibres are mostly arranged in layers placed one in front of the other, with flattened, branching cell spaces and cells between them. The cell spaces are sharply defined by the silver nitrate after removal of the epithelium from the corneal surface (Fig. 60). They are branched, and freely anastomose. The nuclei of the cells may be seen after silvering. The method, however, is not suitable for revealing the protoplasm. But the method of staining with chloride of gold brings the branching network of cells, with their relatively large nuclei, completely into view (Fig. 61, *a*). When the cornea thus stained is sliced vertically at right angles to its surface, it is seen that the cells are flattened between the fibrous bundles (*b*). In addition to these, the fixed or proper corneal corpuscles, wandering cells occur here and there in the cell spaces. They probably come from the blood-vessels at the margin of the cornea; at all events it is certain that when the cornea is irritated white blood-corpuscles do migrate from the blood-vessels at the periphery into the interior of the cornea.

Development of White Fibrous and Elastic Tissue.—All the forms of connective tissue are developed from the mesoblast, and, as already stated, mucous tissue is the predecessor of ordinary connective tissue. The first indication of its transformation into ordinary connective tissue is indicated by the appearance of white fibres in the jelly-like matrix, distinct from the cells (Ranvier), but often lying very close to them. As age advances the cells multiply in number, in a manner not fully ascertained; judging from what may be seen in the tail of the tadpole (Fig. 14), very many of the cells are emigrated white blood-corpuscles. Schwann stated that the connective tissue cells are at first rounded (Fig. 62, *a*). They become elongated (*a′ a″*), and the cell envelope splits into a bundle of fibrils (*a‴*). Beale showed that there is no envelope, and maintained that the outer part of the protoplasm is changed into a "formed material," which becomes a bundle of white fibrils. But without denying the possibility of this, we must admit, with Ranvier (*Op.* 39, p. 410), that we have entirely failed to find any certain evidence of it. But it is very easy to find appearances that at first sight seem to support Beale's view. The real mode of development appears to be thus: A periplast is produced by the cell mostly on only one of its flattened surfaces. The periplast elongates, probably by an interstitial growth, like the periplast of a Tradescantia cell (Fig. 5), and eventually becomes a white fibre; but the flattened cell, although it may appear continuous with the substance of the fibre, is in reality separable (Fig. 63, *c*), and when isolated it is easy to see how its thin wings are invisible on the fibre, which therefore looks as if it were a continuation of the body of the cell. According to this view, therefore, the white fibres are just as little a direct transformation of the cell substance here as in white fibro-cartilage and hyaline cartilage. The cell remains as a branched or as an epithelioid connective tissue corpuscle.

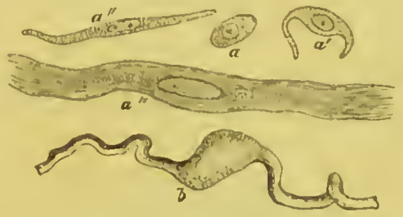

Fig. 62. *a a′ a″*, Elongating cells (Schwann). *a‴*, Cell with a white fibre; *b*, cell with elastic fibre (Beale). × 400.

With regard to the development of the elastic fibres, there has been much difference of opinion. According to Donders (*Op.* 53, iii. p. 354), Virchow, and Beale (*Op.* 54, p. 202), elastic fibres are transformations of the processes of connective tissue corpuscles (Fig. 62, *b*). But although these corpuscles may sometimes be seen in contact with the fibres, we have failed to trace any continuity between them, and therefore agree with Müller (*Op.* 51, x. p. 132) in believing that, as in hyaline cartilage (Fig. 45), they are produced in the hyaline matrix independently of cells, so here they result from the coalescence of particles of elastin between the white fibres, probably in the jelly-like periplast of the original mucous tissue. Sometimes, though rarely, elastic fibres are produced in the substance of a white fibre. The white fibres and the elastic fibres and membranes are, therefore, to be regarded as periplasts.

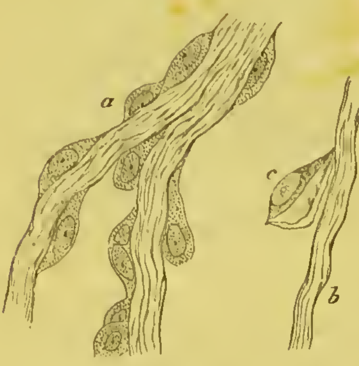

Fig. 63. Young white fibrous tissue from amnion of chick. *a*, Fibres, with numerous cells in close apposition; *b*, fibre with cell, *c*, isolated by teasing. × 400.

Vessels and Nerves of Connective Tissue.—The cornea is devoid of blood-vessels, save its very margin. In tendon and ligament they are few in number. Areolar tissue contains a considerable number in the neighbourhood of fat-cells, or passing through it on their way to adjacent parts, but there are only a few capillaries for the tissue itself. Nor need this be wondered at, considering that the function of the tissue immediately depends on its passive mechanical properties. The great mass of connective tissue is nourished not by pabulum obtained directly from the blood, but from the lymph,—which, as it percolates through the lymph-spaces, bathes the tissue-elements and flows away by the lymphatics.

In the cornea, lymphatic vessels occur in considerable number, and they are numerous in tendon and aponeurosis (Ludwig and Schweigger-Seidel, *Op.* 55). In the central tendon of the diaphragm it can be clearly seen that they open into the lymph-spaces (cell-spaces) of the tissue (Fig. 59), and it is probable that such a communication exists generally throughout connective tissue, so that the lymph-spaces are, as it were, lymph-sinuses between the blood-vessels and the lymphatics. The great serous cavities, *e.g.* the pleura and peritoneum, are, as it were, merely some of the lymph-spaces of connective tissue enlarged for special purposes, and lined by a nearly continuous layer of endothelial plates, that are merely modified connective tissue corpuscles. There is a direct communication between these cavities and lymphatic vessels. It is difficult to know whether the connective tissue cells partially or completely fill the lymph spaces. Probably, in areolar tissue at all events, the spaces are only partly filled by the cells, so that the spaces are easily capable of distension, as in œdema and emphysema.

Tendon and ligament are in their normal states devoid of sensibility, but become extremely painful when inflamed. No nerves have, however, been traced into them. In the cornea there are numerous plexuses of nerve-fibres throughout its substance. Many of the nerves are destined for the highly sensitive anterior corneal surface, but whether or not all are so destined is unknown, but from the richness of the plexuses between the layers of connective tissue it is difficult to believe that some of the nerves are not intended for the connective tissue itself. Nerve-fibres are found in areolar tissue and in aponeuroses, but whether they are intended for the connective tissue itself or for adjacent structures is doubtful.

Irritation of Connective Tissue.—Although it is not the province of this work to teach pathology, nevertheless a passing allusion sometimes requires to be made to pathological events. The account already given (p. 79) of the multiplication of cells consequent upon the irritation of cartilage naturally leads one to expect that the cells of ordinary connective tissue behave similarly when irritated. But the case of ordinary connective tissue is complicated by the fact that, during irritation, blood-leucocytes emigrate from the vessels, gather in numbers amidst the connective tissue corpuscles, and obscure the changes which the latter undergo. Even in the non-vascular cornea this holds true. But although Cohnheim's discoveries regarding the production of pus-corpuscles by the immigration of blood-leucocytes into inflamed parts seemed for a time to upset Virchow's doctrine of their development from connective tissue corpuscles, the truth probably lies between the two—the pus-corpuscles originating in both ways. When the cornea of the frog is irritated with caustic, the nuclei of its fixed cells proliferate and give rise to groups of corpuscles that seem to be those of pus (Hoffmann, *Op.* 19, xlii. p. 204; Norris and Stricker, *Op.* 56, year 1870, p. 1). Also in areolar tissue, when irritated by the injection of silver nitrate solution (1 : 300), its flat cells become in a few hours swollen, and their nuclei proliferate (Ranvier, *Op.* 39, p. 427). The same thing happens in tendon, and it should not be doubted that pus-cells result from the proliferation. But the point we are aiming at is not the origin of pus-corpuscles, but this, that *the fixed connective tissue corpuscle*, after it has become flattened like an endothelial scale, and after its periphery has become, as often happens, a transparent plate, and the whole corpuscle betrays no evidence of germinal power, it, under peculiar conditions, swells, acquires a germinal character, and multiplies. The endothelial scales of serous membranes can behave in a similar manner when irritated. Connective tissue plays a prominent part in many pathological conditions.

BONE.

The most striking feature of bone is its hardness. This property renders it serviceable for protecting delicate organs, such as those in the cranial and spinal cavities, for supporting the limbs and trunk, and for acting as levers for muscular movements. On examining a long bone, such as a rib, it is easy to convince oneself that, although hard, it is not brittle, but tough and elastic. Its hardness is due to calcareous matter, its toughness to fibrous tissue, with which the calcareous matter is intimately united. If the fibrous tissue be destroyed by ignition, the bone preserves its shape unchanged; its hardness remains, but instead of being tough the bone becomes brittle and friable, so that under pressure it crumbles to powder. On the other hand, if the calcareous matter be removed by maceration in dilute hydrochloric or nitric acid, the bone retains its general configuration unaltered, but it becomes so pliable that it may be bent in any direction, sliced with a knife, or torn into shreds.

Structure.

When such a bone as a rib is sawn across, it is seen that towards the surface the bone is *dense* or *compact*, while in the centre it is *spongy* or *cancellated.* The dense merges gradually into the spongy bone, and the spaces in the latter are filled with marrow. Towards the interior of all bones the osseous texture is cancellated. Externally it is compact, except at the joints, where the spongy bone merges into an encrusting layer of cartilage, which, as it were, takes the place of dense bone. In the long bones of the limbs there is in the shaft a large irregular space in the cancellated bone termed the *medullary canal.* In a vertical section of such a bone as the femur it may be observed that in the shaft, where the leverage strain is greatest, the compact bone forms a much thicker layer than at the extremities, where it becomes gradually thinner, until it ceases at the margin of the encrusting cartilage. Towards the articular ends the bone is therefore almost entirely spongy. The general arrangement of the compact and the spongy osseous texture is calculated to combine strength with lightness. The tubular character of the shaft of a long bone enables it to resist a greater lateral strain than could be borne by the same quantity of osseous matter arranged as a solid rod.

Essential Elements of Osseous Tissue.—Osseous tissue essentially consists of nucleated protoplasts imbedded in a periplast chiefly composed of a calcified fibrous tissue. The cell-spaces in which the protoplasts are lodged are termed *lacunæ.* To ascertain the nature and the relations of these elements, it is necessary to study sections of unsoftened bone, made with a saw, and then ground sufficiently thin upon a stone,—and of bone decalcified, *e.g.* by a dilute solution of chromic and nitric acids.

The lacunæ may be most readily seen in thin dried sections of *unsoftened* bone, *e.g.* in a transverse section of the compact osseous tissue of a long bone (Fig. 64). In dried bone they have a black appearance, and are on that account readily recognisable. Like the cell-spaces of the cornea, they are flattened. When seen in section, they are elliptical (*e*), and the length of their greatest diameter is about 14 μ ($\frac{1}{1800}$ inch).

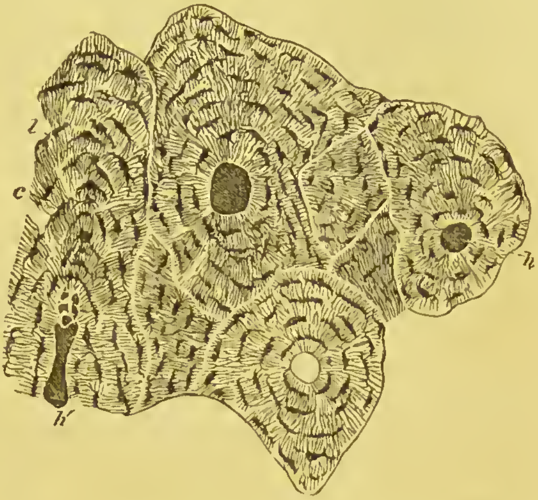

Fig. 64. Transverse section of the compact tissue of a long bone, *unsoftened.* *l*, lacunæ; *c*, canaliculi; *h*, Haversian canal; *h′*, Haversian canal cut obliquely. × 60.

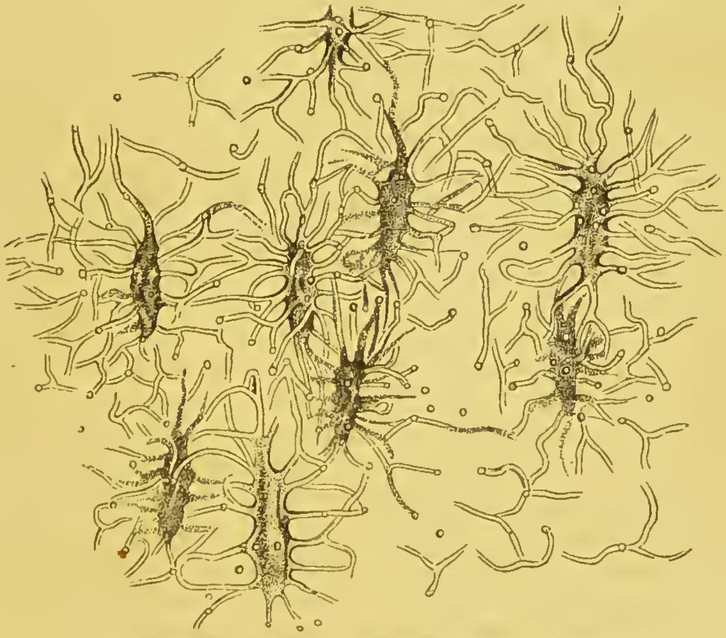

Fig. 65. Lacunæ and canaliculi of unsoftened bone. × 800. (Rollett.)

Neighbouring lacunæ are connected by a system of fine, somewhat tortuous, branching canals (Fig. 65)—the *canaliculi*—that penetrate the calcified fibrous matrix, and probably serve as lymph channels for the irrigation of the nucleated protoplasts in the lacunes, and the osseous matrix (Virchow).

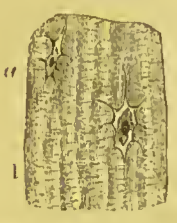

Fig. 66. Transverse section of compact bone f femur, decalcified. *a*, Bone-corpuscle; *l*, lamellæ. × 400.

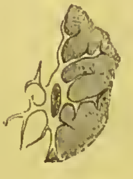

Fig. 67. Bone corpuscle with its branching envelope partially isolated from the surrounding matrix. (Frey.)

The Bone Corpuscles are nucleated protoplasts, and are most readily seen in softened bone (Fig. 66, *a*). They have no processes extending into the canaliculi, but are confined to the lacunæ (Beale); in this respect, therefore, they notably differ from the fixed corpuscles of the corneal connective tissue (Fig. 61).

The Bone Periplast appears to be of a twofold nature. 1. A thin membrane lines the lacunæ and canaliculi, and may be isolated from the surrounding fibrous periplast by dissecting a slice of decalcified bone with needles (Donders, Virchow, *Op.* 51, year 1850, p. 193). The appearances of unsoftened bone suggest that this membrane is calcified. 2. The great mass of the osseous periplast or matrix is a calcified fibrous tissue arranged in lamellæ superimposed like the leaves of a book (Fig. 66, *l*). They are most readily seen in softened, but are also discernible in unsoftened bone. The lamellæ can be readily torn from the surface of a softened long bone. Sharpey, who discovered them, describes a lamella (*Op.* 57, 8th ed. p. 86) as consisting of a fine reticulum of transparent fibres. "The fibres intersect obliquely, and they seem to coalesce at the points of intersection, for they cannot be teased out from one another; but at the torn edge of the lamella they may often be seen to separate for a little way, standing out like the threads of a fringe" (Fig. 68). In some places the fibro-reticular structure is less decidedly marked, as if the fibrillations were incompletely developed. Minute apertures, apparently canaliculi torn across, occur at short intervals in the lamellæ (*c*), and in some there are apertures of considerable size, which constitute the sockets of the perforating fibres of Sharpey (*s*). The lamellæ consist of gelatigenous tissue; the fibres swelling up in acetic acid and yielding gelatine on boiling.

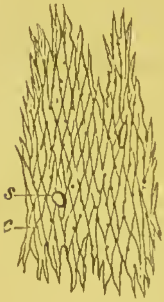

Fig. 68. Lamella torn from a decalcified bone. *c*, Canaliculi torn across; *s*, socket of a perforating fibre. × 400.

When the lamellæ are cut transversely, *e.g.* in a transverse section of a long bone, they may be readily recognised with a power of 300 diam., whether the bone be softened or unsoftened. In the unsoftened bone they have the appearance of thin homogeneous clear bands alternating with layers of a granular-looking substance. The granular appearance of the latter is due to fine bridges of clear tissue that connect adjacent lamellæ. The spaces between these bridges are filled with an interstitial substance, whose contours, mapped by the lamellæ and their connecting bridges, give rise to the granular appearance. In decalcified bone the lamellæ and their connecting bridges stand out more clearly from the interstitial substance (Fig. 66). The interstitial substance, and probably also the lamellæ, are impregnated with calcareous matter. After partial decalcification it may be seen in the form of granules, in the clearly from the interstitial substance (Fig. 66). The interstitial substance, and probably also the lamellæ, is impregnated with calcareous matter. After partial decalcification it may be seen in the form of granules, in the interstitial matter at all events. The lacunæ occur between the lamellæ at varying intervals; from two to five lamellæ usually intervening between neighbouring lacunes.

The above are the essential structural elements of fully-formed osseous tissue. Canals for blood-vessels are only found in thick layers of the tissue, and Sharpey's fibres, that perforate the lamellæ in many situations, are not found everywhere. A description of them is therefore postponed.

Arrangements of Tissues found in an Adult Bone.—Fig. 69 represents a transverse section through one side of a long bone deprived of its periosteum, marrow, and mineral matter. In the *compact bone* (A) there are sections of canals for blood-vessels, termed *Haversian canals* (*c*), after their discoverer Havers. There are also sections of cavities larger than the Haversian canals, named Haversian spaces (*e*). These spaces are most numerous when the bone is young and rapidly growing, but even in adult bone they occur here and there (Tomes and De Morgan, *Op.* 3, year 1853). Both the Haversian canals and spaces contain blood-vessels, connective and other tissues, prolonged inwards from the periosteum. Around each Haversian canal the lamellæ and lacunæ are arranged concentrically: the whole being the transverse section of an osseous cylinder termed a *Haversian system* (*b*). The concentric arrangement of the lacunæ and lamellæ in this system is due to the fact that they are successively deposited from without inwards, in the Haversian spaces, which thus become narrowed into canals. The Haversian systems are of various shapes, according to the outline of the Haversian spaces in which they are formed. The canaliculi of a Haversian system form a freely anastomosing network of lymph channels within the system. Internally, they open into the Haversian canal, and at the periphery of the system some of them anastomose with those of neighbouring systems, but most of them bend back within their own system. These are the recurrent canaliculi of Ranvier. The osseous rods constituted by the Haversian systems mostly run in the direction of greatest strain; thus in long bones they are usually vertical, while in flat bones their direction

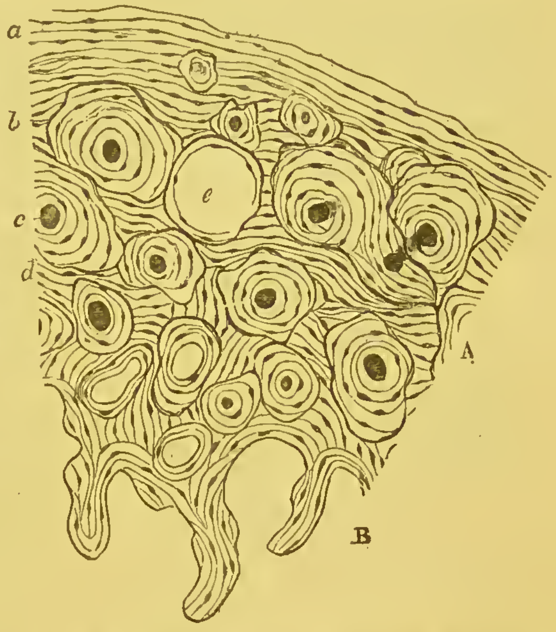

Fig. 69. Transverse section of decalcified femur of cat. A, dense, B, spongy bone; *c*, Haversian canal; *a*, peripheric, *b*, Haversian, *d*, intermediate lamellæ. The cancellous lamellæ are seen around the cancelli. *e*, Haversian space. X 60.

varies according to the requirements. In the *spongy bone* (B) there are large spaces that contain marrow—the cancellous or medullary spaces. These communicate on the one hand with the medullary canal, when it exists, and on the other with the Haversian canals.

The *lamellæ* may be divided into four groups—the *Haversian* (*b*), arranged concentrically around the Haversian canals; the *cancellous*, similarly grouped around the medullary spaces; the *peripheric* (*a*), running parallel with the periosteum; and the *intermediate* (*d*), forming irregular groups between the Haversian systems. Most of the intermediate lamellæ are segments of larger circles than those in the Haversian systems, a circumstance which is explained by the fact that most of the intermediate are remnants of peripheric lamellæ which were produced under the periosteum at an early period in the development of the bone, and which have been encroached on by a process of absorption leading to the formation of Haversian spaces in which the lamellæ of a Haversian system are afterwards deposited. As will afterwards be explained, however, some of the intermediate lamellæ are really remnants of Haversian systems which have been only partially absorbed previous to the formation of the permanent Haversian systems. The Haversian and cancellous lamellæ are both of secondary formation, and are concentrically produced at the periphery of the Haversian and medullary spaces.

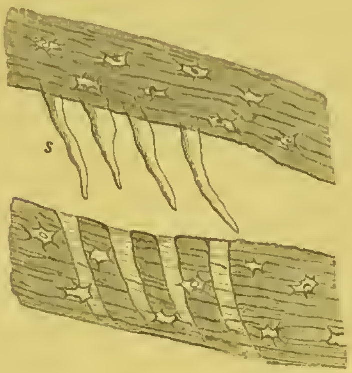

Fig. 70. *s*, Sharpey's fibres torn from their sockets by separating the peripheric lamellæ of a softened femur. × 250.

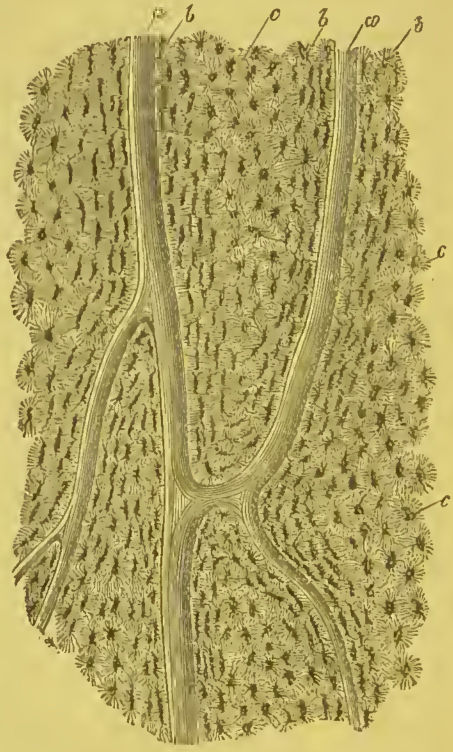

Fig. 71. Vertical section of compact tissue of a long bone. *a*, Haversian canals; *b*, lacunæ; *c*, canaliculi. × 100. (Kölliker.)

Sharpey's Fibres.—The peripheric and intermediate lamellæ are pierced by fibres termed *perforating* or *Sharpey's fibres.* They may be recognised with a power of 200 diam. in such a section as that under consideration (Fig. 69), but they become most evident when the peripheric lamellæ are torn asunder with the aid of needles, for then the fibres are pulled out of their sockets (Fig. 70). Usually, however, this cannot be accomplished to any great extent, for the fibres often form networks within the bone. Most of them are of the nature of white fibrous tissue, whilst some are elastic (H. Müller). The latter may be distinguished by the circumstance that magenta stains them of a dark red colour, whilst the white fibres are unaffected (Schäfer, *Op.* 8, xviii. 136). Many of the fibres, but not all, are calcified. Sharpey states that they are rarely found within a Haversian system; but according to Ranvier (*Op.* 39, p. 308) they are never found there, and occur only in the peripheric and intermediate lamellæ—these being formed directly from the periosteum. In the opinion of Sharpey, these fibres are merely a modification of the mechanical structure of the tissue, and seem to have no physiological significance. They are best seen where a tendon is attached to the bone, and it may be fairly assumed that they strengthen the attachment.

The appearance of a longitudinal section of the compact tissue of a long bone (Fig. 71) differs widely from one that is transverse. The Haversian canals are seen running longitudinally and anastomosing one with another. On the one hand these canals open more or less obliquely under the periosteum, from which their blood-vessels are derived, and on the other they communicate with the medullary spaces in the spongy bone.

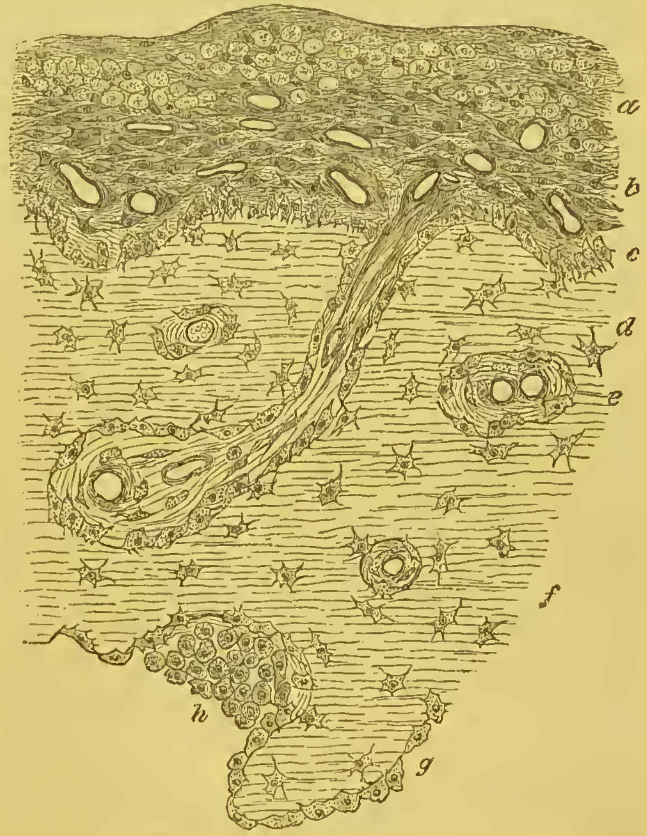

Fig. 72. Transverse section of decalcified femur of kitten four days old; drawn after staining with picrocarmine. *a*, Outer layer of periosteum with connective tissue bundles cut transversely and longitudinally; *b*, inner layer with proliferating connective tissue corpuscles; *c*, osteoblasts; *d*, longitudinal, *e*, transverse section of Haversian canals; *f*, osseous tissue; *g*, osteoblasts lining cancelli; *h*, medullary cells. Blood-vessels cut longitudinally and transversely are seen in the Haversian canals and periosteum. × 400. (Reduced.)

THE PERIOSTEUM is a fibrous membrane (Fig. 72), forming an external covering to the bones. It may for convenience be divided into two layers, although there is no sharp line of demarcation between them: an *outer layer* (*a*) composed of numerous elastic and white fibres, mostly running longitudinally; and an *inner layer* (*b*) that is structurally different in the young as compared with the adult state. In the young growing bone it consists of a delicate fibrous tissue, with numerous cells imbedded in the mesh-work and forming a distinct layer upon the surface of the bone (*c*). Those in contact with the osseous tissue, being immediately concerned in its growth, were named by Gegenbaur *osteoblasts.* As age advances the inner layer of the periosteum becomes more fibrous, and the osteoblasts fewer in number (Fig. 73). White and elastic fibres pass from the periosteum into the bone, and constitute the perforating fibres. The periosteum is an exceedingly vascular membrane, most of its blood-vessels being destined for the bone. It also contains numerous lymphatics and nerves, many of which accompany the blood-vessels into the bone.

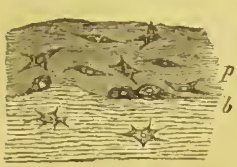

Fig. 73. *p*, Inner layer of periosteum of femur of adult cat; *b*, osseous tissue. × 400.

The deeper layer of the periosteum is prolonged into all the Haversian canals. In a vertical section of one of these in a softened bone, the vessels, connective tissue, and osteoblasts, may be readily seen if the bone be young (Fig. 72, *d*); but in adult bone the osteoblasts are few in number. A Haversian canal therefore contains blood-vessels, fine connective tissue, osteoblasts, together with lymphatics and nerves. On the inner aspect of the bone the canals open into the medullary spaces of the spongy bone, and the osteoblasts and vascular connective tissue are prolonged through the canals into the cancelli. Everywhere in the interior of the cancelli of spongy bone, and the medullary canal of a long bone, there is a layer of cells, mostly osteoblasts (Fig. 72, *g*), but in spongy bone, particularly in that which is young, these are here and there replaced by large multinucleated giant cells, which, according to Kölliker, are concerned, not in the formation, but in the absorption of bone, hence he has named them *osteoclasts* (Fig. 79, *oc*). In the medullary canal of a long bone the vascular fibrous tissue in contact with the bone forms a sort of membrane, that has received the special name of *endosteum.*

THE MARROW of bone is either yellow or red. *Yellow marrow* occurs in the medullary canal, and larger cancelli of long bones. It chiefly consists of fat-cells and blood-vessels, with some connective tissue. *Red marrow* occurs in the spongy tissue at the ends of the long bones of the limbs, in the clavicle, ribs, and in all the flat and short bones. It consists of a delicate connective tissue, with many blood-vessels and a great number of cells, most of which are the *medullary cells* or proper marrow cells of Kölliker. They are all nucleated protoplasts, many of them exactly resembling lymph-corpuscles (Fig. 74, *g*, *d*), while others have a single large nucleus, with a nucleolus (*c*). Others closely resemble these, but contain fatty particles, and appear to be young fat cells (*e*); red marrow, however, contains very few fat cells. There are many red blood-corpuscles (*b*), but they probably belong to the blood within the vessels of the marrow.

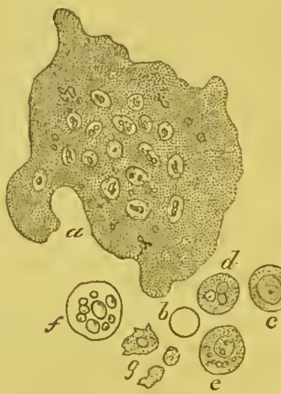

Fig. 74. Corpuscles found in red marrow from rib of dog. *a*, Giant cells; *b*, coloured blood-corpuscle; *c*, *d*, *e*, *f*, *g*, medullary cells. × 300. (The nuclei of the cells were rendered evident by dilute alcohol.)

Neumann and Bizzozero (*Op.* 23, year 1868, pp. 689, 885) state that in red marrow there are *nucleated* red blood-corpuscles similar to those found in the embryo (Fig. 23A). From this they conclude that in red marrow, white corpuscles develop into coloured blood-corpuscles, and that, in short, it is to be regarded as a blood gland. Ranvier (*Op.* 39, p. 324) has failed to find these corpuscles, and has cast doubt on Neumann's observations; but, on the other hand, their accuracy is supported by Rindfleisch in a recent memoir (*Op.* 18, vol. xvii. p. 1). One must be careful not to mistake for such corpuscles the nucleated cells with yellow granules (*e*), which are blackened with osmic acid, and are therefore fat. Further investigation, however, is needed ere definite conclusions can be arrived at regarding the significance of the medullary cells.

Osteoclasts are large multinucleated masses of protoplasm (Fig. 74, *a*). In the bone of a young subject they may be found in considerable numbers, but scarcely at all in that of an adult. They, together with osteoblasts, lie in contact with the bone in the cancelli (Fig. 79, *oc*, *ob*), and can scarcely be regarded as constituents of the marrow proper.

NUTRITION OF BONE.—The blood-vessels of the Haversian canals enter from the periosteum at all parts of the surface of the bone. Some of them pass through the compact bone into the cancelli, and thus supply blood to the medulla. In the long bones these medullary vessels are numerous near the articular extremities; and in the shaft there is a canal that transmits an artery of considerable size into the medullary cavity. This, the so-called "nutrient artery," gives only a few branches to Haversian canals in its passage through the bone, and chiefly ends in the medulla. Since the osseous tissue is nourished by vessels that enter everywhere from the periosteum, it is apt to die if this membrane be stripped off. This always takes place if the denudation be extensive. In the adult, even a very partial denudation is apt to be followed by superficial necrosis; in the young subject this result is less frequent, probably because of the greater relative size of the Haversian canals, and therefore, it may be, freer collateral circulation within the bone. The veins of bone have a distribution similar to that of the arteries. In the cancelli they are numerous and much dilated. In compact bone they have pouch-like dilatations, and sometimes occupy canals distinct from those containing the arteries (Todd and Bowman). Often, however, both occur in the same canal (Budge, *Op.* 24, v., Abtheil. 1, p. 99). The tolerably large openings near the ends of the bone are mostly venous canals. There are valves in the veins where they leave the bone (Langer, *Op.* 24, v., Abtheil. 1, p. 97). Within the marrow, the blood-vessels form a closed system (Langer, *op. cit.*). Most of the vessels have few or no muscular fibres. In the Haversian canals their walls are so thin that they may be supposed to readily permit of the transudation of lymph.

Lymphatics accompany the blood-vessels from the periosteum through the Haversian canals into the medullary spaces and medullary canal. They may be injected by the puncture method, either from the periosteum (Budge, *Op.* 24. v., Abtheil. 1, p. 99) or from the medullary canal (Schwalbe, *ibid.* p. 101). In the Haversian canals and cancelli the lymphatics surround the blood-vessels and constitute a space that is lined by a layer of endothelium. According to Budge's observations (*op. cit.*), the lymphatics are in direct communication with the lymph spaces in the connective tissue of the marrow, and with the canaliculi of the bone.

The nerves of bone accompany the blood-vessels (Kölliker), but nothing has been ascertained with regard to their ultimate distribution. The general absence of muscular fibres from the walls of the vessels must be borne in mind in this connection, for on that account the nerves are probably to a very small extent to be regarded as motor for the blood-vessels. In its normal state, bone is very slightly sensitive, but it becomes extremely so when inflamed. Violent irritation of the medullary tissue produces pain.

Chemistry of Bone.

Bone contains an extremely small quantity of water. The solids consist of about one-third organic, and two-thirds earthy matter. The composition of dried compact bone is stated by Berzelius to be as follows:—

Organic matter		33·30
Mineral matter	Calcium phosphate	51·04
	„ carbonate	11·30
	„ fluoride	2·00
	Magnesium phosphate	1·16
	Sodium salts	1·20

The composition varies somewhat in different bones; thus, in the temporal there is more earthy matter than in other bones; hence, its extreme hardness. There is also more in the bones of the extremities than in those of the trunk; more in the humerus and femur than in the bones of the forearm and leg; more in the ilium than in the scapula (Rees).

The following analyses by Fremy of the compact substance of the femur show that at various ages the organic matter remains almost exactly the same, except in the fœtus, where its amount is somewhat greater.

		Organic matter.
Female	fœtus	37·0 per cent.
„	newly-born	35·2 „
„	22 years of age	35·4 „
„	80 „	35·4 „
„	81 „	35·5 „
„	88 „	35·7 „
„	97 „	35·1 „

With advancing age, bone becomes more brittle. This is possibly the result of a molecular change in its fibrous tissue.

The organic substance of osseous tissue consists of the nucleated corpuscles and fibrous tissue. The chief organic element is of the nature of white fibrous tissue, from which gelatin can be extracted by boiling. This result is most striking when decalcified bone is boiled; although decalcification is not necessary as a preliminary step to obtaining the gelatin. Unsoftened bone also yields it to boiling water. The organic matrix has been named *ossein*, a term that is entirely superfluous. The chief mineral constituent of bone is calcium phosphate, having the formula $Ca_3(PO_4)_2$. It has been surmised that the earthy salts are not merely infiltrated in the organic matter, but are in a state of chemical union with it (Zalesky). The separability of the organic part by boiling water, however, seems to be opposed to this idea.

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Development of Bone.

In most situations, bone is preceded by hyaline cartilage; but the clavicle, facial bones, and flat bones of the skull are preceded by fibrous membrane. Accordingly two modes of bone-development are recognised —the *intracartilaginous* and the *intramembranous.* In all bones preceded by cartilage, one portion is produced in the cartilage and the other in fibrous membrane. The formation of the bony skeleton begins with the clavicle, about the seventh week of fœtal life.

FORMATION OF A LONG BONE.—Any growing long bone may be taken as an example of ossification where the bone is preceded by cartilage, and it is convenient that we study first the intracartilaginous part of the process.

Intracartilaginous Ossification.—Previous to the appearance of the osseous tissue in such a bone as a phalanx (Fig. 75), its place is occupied by a rod of hyaline cartilage, shaped like the future bone, and enclosed in perichondrium. The perichondrium in time becomes the periosteum; the hyaline matrix of the cartilage disappears everywhere, save at the articular ends of the bone. What becomes of the cartilage cells will presently be considered.

The ossification begins in the middle of the shaft of the phalanx, about the fourth month of fœtal life, and extends towards the extremities. The first step towards ossification consists in proliferation of the cartilage cells and infiltration of the cartilage matrix with lime salts. The cells enlarge and repeatedly divide more or less transversely to the long axis of the phalanx, and thus give rise to longitudinal rows (*c*). At first the cells, after division, secrete a capsule, that becomes fused with the surrounding matrix; but after a time the cell-division takes place so rapidly, that groups of cells are formed within a single capsule. The cavities containing them grow larger by absorption (Fig. 76, *a*, *b*), and eventually become the medullary spaces of the embryonic bone. At the same time the character of the cells undergoes an important change, for they cease to produce capsules, and become not unlike the medullary cells of bone. While the cells are multiplying, lime salts are deposited in the matrix, apparently for the purpose of enabling it to resist the effects of external pressure, notwithstanding the relative increase of its soft cellular elements. The calcified matrix does not, however, become the matrix of the future bone, but entirely disappears, as Sharpey first pointed out.

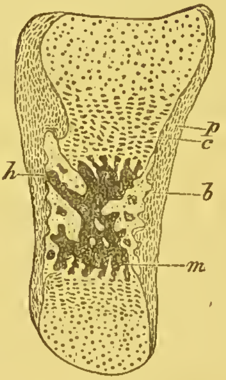

Fig. 75. Ossification in phalanx of human fœtus at about fourth month. *p*, Perichondrium; *c*, cartilage cells in rows; *b*, young bone; *h*, Haversian canal; *m*, medullary spaces. × 20. (Reduced.)

Blood-vessels, accompanied by processes of perichondrial connective tissue, now penetrate the cartilage. They appear, by their growth, to cause absorption of the matrix, and thus find their way into the spaces containing the proliferated cartilage cells. The blood-vessels then grow towards the ends of the phalanx, causing absorption of its matrix, and finding their way into more and more of the cell-spaces. It cannot be said that the absorption of the cartilage matrix is entirely owing to the blood-vessels. It is in large measure due to the proliferation of the cartilage cells. Indeed a coalescence of cell cavities may sometimes be seen (Fig. 76, *c*), when no blood-vessels can be discerned within them. The coalesced cell-cavities of the cartilage constitute the primary medullary spaces of the future bone. They contain blood-vessels, a very delicate connective tissue, and many cells, some of which are liberated cartilage-cells, others are probably white blood-corpuscles that have emigrated from the vessels (Frey), while some may be descendants of corpuscles in the perivascular processes of connective tissue that grow inwards from the perichondrium (Lovén). As we have not found it possible to trace the ossifying process farther in the specimens of human bone at present in our possession, we must turn to a vertical section of the head and shaft of a long bone, *e.g.* the humerus of a rabbit, kitten, or pig, made when the ossifying process has advanced towards the articular ends of the cartilaginous rod. As the changes in the cartilage here slightly differ from those observable at the centre of the human phalanx, it will be necessary to recapitulate some part of what has been said, and to study in their order of succession all the stages of the ossifying process observable in such a section (Fig. 76 A).

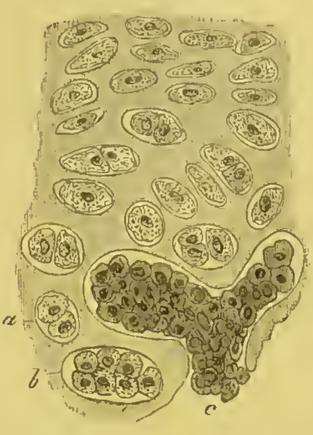

Fig. 76. Cartilage of phalanx of fœtus æt. four months, near point of ossification in centre of shaft. *a*, *b*, *c*, Successive stages in the formation of primary medullary spaces. × 300.

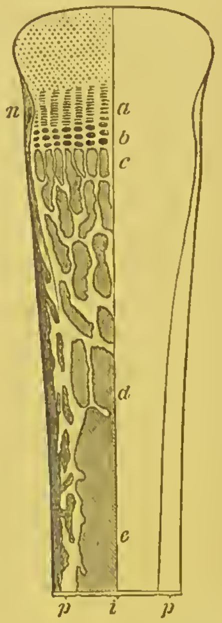

Fig. 76A. Vertical section of the end and shaft of a growing long bone of a rabbit. *a*, Zone of proliferating cartilage cells; *b*, zone of enlarged cells; *c*, primary medullary spaces; *d*, enlargement of medullary spaces by absorption; *e*, medullary canal; *i*, the part of the bone formed in cartilage; *p*, the part formed in periosteum; *n*, notch where the periosteum grows in length. *Partly schematic.* Low magnifying power.

In the part of the cartilaginous extremity near the bone the cells grow somewhat larger, actively divide, and form longitudinal rows (*a*). Each cell continues to secrete matrix, and this becomes calcified.

Still deeper (*b*), the cells become three or four times larger than in the preceding zone, and on that account the matrix is partly absorbed. But here, unlike the central part of the human phalanx, the proliferated cells do not form groups inside a common capsule, nor do the cells occasion a coalescence of cell-cavities.

Below the zone of enlarged cells a series of primary medullary spaces (*c*), containing capillaries and many cells (Fig.

77, *m′*), occupy the sites of the rows of cartilage cells, the transverse septa of which have been absorbed, apparently by the growth of the capillaries (*v*) in the medullary spaces (Ranvier, *Op.* 39, p. 438). The cartilage cells thus liberated *seem to break down* (*c′*, *c″*); at all events, their appearance here is very different from that in the human phalanx, where there is no evidence of their degeneration. The cells in the medullary spaces in this situation are therefore to be regarded as either emigrated white blood-corpuscles (Frey), or connective tissue corpuscles (Lovén). Some of the medullary cells become giant cells, which apply themselves here and there to the trabeculæ of calcified matrix by which the spaces are laterally bounded. These play the part of *chondroclasts*, causing absorption of the cartilage with which they are in contact, so that the spaces are enlarged and their intercommunication increased. The trabeculæ of calcified cartilage constitute a framework that enables the cartilaginous rod to resist external pressure and retain its shape while it is being excavated and replaced by bone.

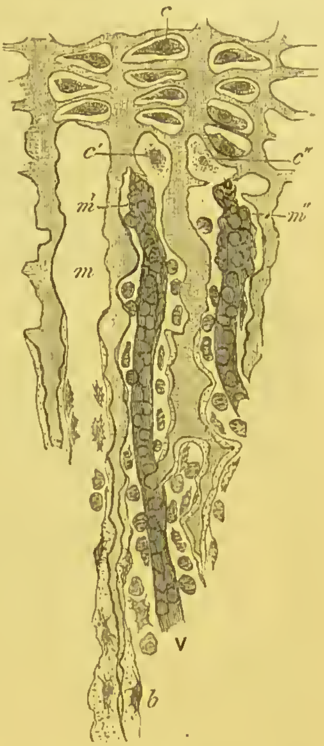

Fig. 77. Vertical section of cartilage between the epiphysis and the shaft of a growing long bone of rabbit. c, c′, c″, Cartilage cells; m, m′, m″ primary medullary spaces; v, blood-vessel; b, young bone. × 300. (Drawn after softening with dilute chromic and nitric acid, and staining with picro-carmine.)

The trabeculæ ere long become encrusted with a thin layer of osseous tissue (*b*), and primary cancellated bone results. The osseous texture is produced by osteoblasts—nucleated protoplasts that are either transformed connective tissue corpuscles, or white blood-corpuscles.[1] They assume a somewhat elongated and branched shape when about to become bone-cells. Their processes usually first appear on the side where the osseous matrix is first produced, but sometimes the whole cell becomes branched ere it is embedded (Fig. 78). The bone matrix is a periplast produced by the osteoblasts. Unlike the periplast of cartilage, it does not make its appearance simultaneously all around the cell, but is first seen between the osteoblast and the cartilage-trabecula (Fig. 77, *b*), and from thence grows up around the osteoblast, and envelopes it, so that the osteoblast becomes a bone-corpuscle. In due time fresh osteoblasts at the surface of the young bone produce osseous matrix, and in turn become enveloped. It is maintained by Beale (*Op.* 54, p. 255) that the osteoblasts do not become branched, and that the canaliculi are merely spaces left in the growing bone. That spaces in the periplast are left for the canaliculi seems perfectly correct, yet we have a difficulty in accepting this view of the development of the canaliculi, for Fig. 78 is a correct copy of a preparation, and it shows osteoblasts with processes before they are enveloped in the bone. The theory readily suggests itself, that these processes become canaliculi; that the calcified envelope of the lacuna and canaliculi is either a transformation of the outer part of the protoplasm, or a secretion from it, and that the protoplast eventually retires into the central part of its branched envelope. It is probable that some canaliculi are formed by absorption after the bone-cells are embedded. It cannot, however, be maintained as yet that the development of the canaliculi is sufficiently understood. As the layer of young bone thickens on the trabeculæ of cartilage, the latter to a large extent disappear by absorption.

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[1] H. Müller's opinion that cartilage cells become osteoblasts receives some measure of support from the appearances of the liberated cartilage cells in the human phalanx (Fig. 76), while, on the other hand, Lovén's denial of this origin is supported by the appearances which the liberated cartilage cells present in the rabbit (Fig. 77, *c′*). Lovén maintains that they spring from connective tissue corpuscles.

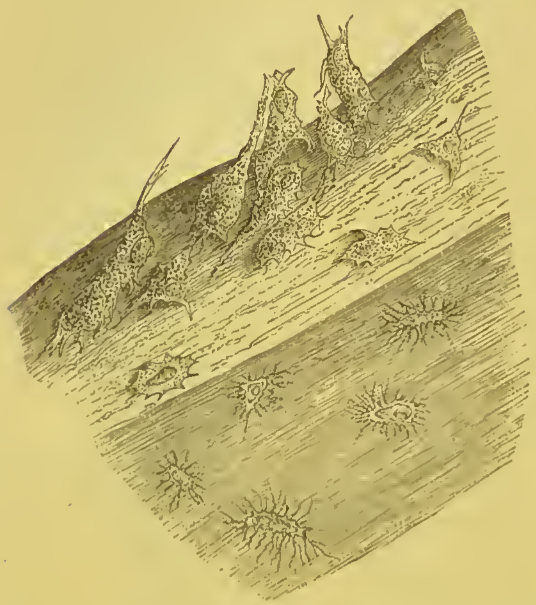

Fig. 78. Oblique section of decalcified cancellated bone of cat, showing osteoblasts on the free surface of the bone (above). The bone-corpuscles are seen in the bone below. × 800.

For a time, the trabeculæ of the primary spongy bone grow thicker by the superposition of new layers of osseous tissue. Were this to continue indefinitely, the primary medullary spaces would be in danger of occlusion, but this is prevented by the production of giant cells, which enlarge the spaces (Fig. 76A, *d*) by here and there absorbing portions of the intervening trabeculæ; and in bones where a medullary canal is formed, these cells completely remove the primary osseous texture in the middle of the shaft (*e*).

After the diaphysis (shaft) is ossified, one or more independent centres of ossification are formed in its cartilaginous extremities. The appearance of these is heralded by the inward growth of vascular periosteal processes, just as at the centre of the shaft. The elongation of the bone then continues in the cartilaginous plate between the epiphysis and the diaphysis. The cartilage grows with such rapidity that, notwithstanding its incessant partial disappearance in the ossifying process, a layer of it persists in that situation until the bone has grown to its full length, when it disappears everywhere save at the articular extremities. That the elongation of the long bones of the limbs takes place at the ends, and not interstitially, was proved by Hales, and also by Hunter and others, who bored holes and inserted shot or ivory pegs at a measured distance apart in the shaft of a long bone of a young animal, and found after a time that, although the bone had grown longer, the interval between the pegs had not increased.

It is instructive to compare the behaviour of the cartilage *above* the epiphysis with that of the cartilage *below* it. As previously described (p. 78), the cells in the cartilage near the bone form by division linear series, and the matrix becomes calcified. Probably this is the extent of the change ; but here and there near the bone, cells may be seen (Fig. 40, *d*) enveloped in a thin layer of osseous matrix continuous with the bone, suggesting that the cartilage cell had ceased to secrete the periplast of cartilage and had produced the periplast of bone. This appearance, however, is probably in reality due to an invasion of the cartilage matrix here and there by bone-corpuscles produced in medullary spaces in the manner already described.

Intramembranous Ossification.—While the above changes are taking place in connection with the cartilage of the growing bone, the perichondrium becomes periosteum, and largely participates in the ossifying process; indeed the thickening of the bone is due to its influence. The earliest change in the perichondrium consists in the direct transformation of its inner part into bone.[1] Its fibrous matrix becomes calcified, and its corpuscles transformed into bone-cells. After a time, however, the connective tissue corpuscles proliferate rapidly, and thus the inner or osteogenic part of the periosteum, with its layer of osteoblasts on the bone, comes about (Fig. 72, *b*, *c*). The bone grows outwards in the fibrous membrane by the superposition of osseous lamellæ with their included bone-corpuscles. The osseous matrix is produced by the osteoblasts in the form of clear fibres, which by their interlacement produce the lamellæ. These fibres appear to be identical with the osteogenic fibres first described by Sharpey in intramembranous ossification as exemplified in the parietal bone (Schäfer, *Op.* 8, xviii. p. 141). They appear to be a periplast specially formed by the osteoblasts, and not a transformation of the fibrous matrix of the periosteum. At the same time, however, periosteal fibres do become included in the bony matrix, and constitute Sharpey's fibres, most of which become calcified. Near to the ends of the diaphysis a thin layer of cartilage separates the endochondral from the periosteal bone, but after a time this disappears, so that the latter lies in contact with the bone formed in cartilage, and it is scarcely possible to distinguish the one from the other. The crust of periosteal bone strengthens the shaft, while the excavations for the medullary canal and permanent cancelli are proceeding within. Around the neck of the articular cartilage there is a shallow circular furrow or notch (Fig. 76A, *n*), in which an active proliferation of the periosteal cells occurs, whereby the elongation of the periosteum appears to be effected.

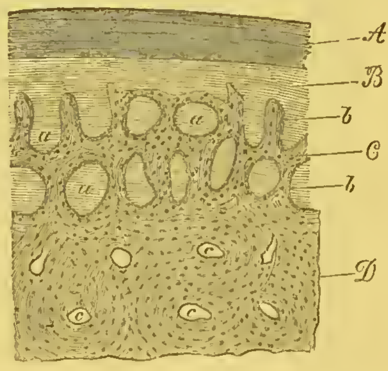

Fig. 78A. Transverse section near the surface of the diaphysis of the metatarsal bone of a calf. *A*, *B*, outer and inner periosteal layers; *C*, primary spongy bone; *b*, trabeculæ; *a*, Haversian spaces; *D*, dense bone with Haversian canals (*c*). × 45. (Kölliker.)

The young periosteal bone has a spongy character, owing to the growth of the osseous texture in the form of trabeculæ (*c*, Fig. 78A). As these extend outwards they include processes of the deeper periosteal layer, with its vessels, connective tissue, and osteoblasts. The cavities in the osseous areola are Haversian spaces (*a*), which become narrowed into Haversian canals (*c*) by the deposition of bone in their interior. On the inner aspect of the periosteal bone, however, these canals are widened into the permanent medullary spaces of cancellous bone by a process of absorption.

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[1] From an unpublished thesis by Dr. De Burgh Birch.

Duhamel (1739), a French naturalist, first conceived the idea that bone grows from the periosteum, as an exogenous stem grows from the inner layer of its bark. It had been previously discovered accidentally by Belchier that when madder is mixed with the food of young pigs, the parts of their bones produced during its administration acquire a red colour. Duhamel repeated the observations, and found that in young animals fed on madder a coloured ring of bone appeared under the periosteum. Numerous observations made since his time show that the madder everywhere stains the growing bone, so that the ends of the shaft under the epiphysis, and a layer of bone under the periosteum and around each Haversian space and canal, is reddened by the dye, that attaches itself to the calcium phosphate, for which it has a marked affinity. Syme (*Op.* 5, year 1840, xiv. 162), however, appears to have been the first to give practical effect to Duhamel's discovery, by showing that if a silver plate be inserted between the periosteum and the bone of the radius of a dog, the periosteum produces a layer of bone outside the plate; and he further proved that bone may be regenerated after its removal, provided the periosteum be left. Ollier (1867) (*Op.* 60) also showed that the periosteum produces bone even when it is excised and planted beneath the skin.

FORMATION OF THE MEDULLARY CANAL, PERMANENT CANCELLI AND MARROW.—In a long bone, such as the femur, all the osseous tissue first produced is afterwards removed by absorption; the site of the embryonic femur being the medullary canal of the adult bone. All the shaft of the permanent bone is therefore produced by the periosteum, while only its extremities are developed in cartilage.

While the production of tolerably compact bone is going on under the periosteum, so that a strong supporting shell of bone is always maintained, excavation takes place in the interior, and leads to the formation of the medullary canal and permanent medullary spaces. Howship was the first to observe the presence of minute pits on the fangs of the milk-teeth during their absorption, and also on the surface and in the interior of bone wherever absorption may be taking place. These pits were consequently named Howship's lacunæ by Lieberkühn, but the term *Howship's foveolæ* is less ambiguous, and therefore preferable. Tomes and De Morgan (*Op.* 3, year 1853) discovered cells in these foveolæ, and advanced the theory that the excavation of the adjacent bone is due to its absorption by the cells. The cells in question are those more recently named myeloplaxes by Robin, and osteoclasts by Kölliker (*Op.* 62). They are multinucleated protoplasts (Fig. 74, *a*) devoid of contractility (Bizzozero, quoted in *Op.* 62, p. 22). They have no envelope, and rarely any processes. In some instances a part of their periphery resembles the striated border of intestinal epithelial cells. They lie in contact with, and are usually somewhat flattened against, the bone (Fig. 79, *oc*), which is mostly pitted as if excavated by them. The manner in which they induce absorption of the bone is unknown, but very possibly it is by a process analogous to digestion. Osteoblasts and osteoclasts may, in a young bone, often be seen in relation to adjacent parts of bone in the same medullary space (Fig. 79). After feeding with madder, a layer of reddened bone is seen under the *osteoblasts, but not under the osteoclasts, showing that the former, and not the latter, are concerned in the production of bone.*

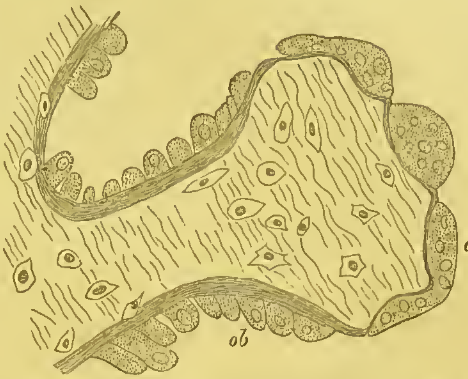

Fig. 79. Section of cancellated bone of lower jaw of calf—decalcified, and drawn after carmine-staining. *ob*, Osteoblasts in contact with a layer of young bone, shaded to indicate that it was stained; *oc*, osteoclasts in Howship's foveolæ. (Kölliker.)

Nearly the whole of the endochondral—and much of the periosteal—part of a long bone is removed by osteoclasts, to make room for the medullary canal and permanent cancelli. In the young periosteal bone they may enlarge the Haversian spaces, or reconvert Haversian canals into wide spaces, by eating away the Haversian lamellæ partially or completely, and they may also partially or completely remove the intermediate lamellæ in the bone that is to be permanently compact, as well as in that which is to remain permanently spongy. After a time, however, the process of absorption ceases, osteoblasts reappear, Haversian and cancellous lamellæ are again produced, and the compact and spongy bone assume their permanent characters. In the outer periosteal bone, which is to be permanently compact, many of the Haversian systems first produced are excavated by absorption, and new systems laid down in enlarged cavities (Fig. 69, *e*), probably for the purpose of replacing the intermediate lamellæ to a large extent by rods of concentric lamellæ running in the direction of greatest pressure.

As regards the origin of osteoclasts, Kölliker (*Op.* 62, p. 26) maintains that they are developed from osteoblasts, the nuclei of the latter proliferating, and the physiological character of the protoplasm undergoing a profound alteration. Rindfleisch (*Op.* 63, ii. 288) and Bredichin (*Op.* 23, year 1867, p. 563) are of opinion that they may arise from bone-corpuscles, the surrounding bone becoming absorbed, and the osteoclasts liberated into the medullary spaces. Regarding the fate of the osteoclasts, Kölliker believes that they divide into osteoblasts and medullary cells. Frey (*Op.* 64) is disposed to doubt that bone-absorption is effected by cells, but as he gives no adequate reason for his doubts, and advances no better theory, we prefer to support the view suggested by Tomes and De Morgan, and elaborated by Kölliker.

It has been already stated that the cells in the primary medullary spaces may be emigrated white blood-corpuscles, connective tissue corpuscles, or liberated cartilage cells. The medullary cells of the permanent spaces are doubtless in large measure descendants of those of the primary spaces. Some of them, however, are possibly bone-corpuscles liberated by the process of absorption, and it has been already stated that some of them may result from the division of osteoclasts (Kölliker). The fat cells of marrow appear to be developed from the medullary cells (p. 100).

FORMATION OF THE PARIETAL BONE.—The parietal bone may be taken as an example of those bones—viz. the flat bones of the skull, the bones of the face, and the clavicle—which are entirely formed in fibrous membrane. The absence of any pre-existing cartilage in these cases was first pointed out by Nesbitt (*Op.* 61); but the process of ossification in these parts was first described by Sharpey. The first stage of the process is somewhat obscure, but it seems to consist in the multiplication of connective tissue corpuscles, and the conversion of these into osteoblasts, as happens under the periosteum. The osteoblasts become bone-corpuscles, and secrete the substance of the osteogenic fibres which become lamellæ, and in their growth include pre-existing fibres of the connective tissue as Sharpey's fibres. The surface of the young bone is covered with osteoblasts, and the mode of its formation is similar to that already described in the periosteum of a long bone. The edge of the growing bone is jagged, owing to the pointed bony processes that grow into the surrounding membrane; vascular processes of the periosteum are included; Haversian spaces are thus formed, and the subsequent transformation of these into Haversian canals and cancelli comes about in the same way as under the periosteum of a long bone.

It is evident that the development of bone is altogether a very singular process. The manner in which the cartilage grows, and yet disappears,—the device by which it is strengthened during its excavation,—the formation of a bony scaffolding around the cartilaginous framework, and the subsequent removal of both,—the formation of a periosteal bony shell around the endochondral bone,—its manner of increasing externally while its excavation proceeds within,—the construction, resolution, and reconstruction which enable a bone to grow in length and thickness, while with increasing size it preserves a comparatively light and spongy core with a firm resisting exterior,—all constitute a very remarkable series of developmental changes that are of great significance in assisting us to form just conceptions of the physiological powers of cells.

CHAPTER IX.

ADIPOSE TISSUE.

ADIPOSE tissue is found in all vertebrates, and consists of cells whose function is the secretion of fat. The fat accumulates in their interior, and constitutes a store that is drawn upon as the needs of the economy require. It is developed amidst areolar tissue, and is widely distributed throughout the organism. It principally occurs in the deeper layer of the skin, around the synovial membrane of the joints, in the mesentery and omentum, underneath the pericardium, in the orbit, and in the bones. It is not, however, found within the cranium, or between the bladder and rectum, or in the subcutaneous tissue of the eyelids.

STRUCTURE AND CHEMISTRY.—Fat cells, when free, are more or less spherical (Fig. 80), when pressed together they are polyhedral. They vary in size from 40 to 80 μ, and consist of a thin colourless envelope, enclosing a mass of yellow fat, which, in the fully formed cell, usually constitutes the chief part of its bulk. There is always a nucleus placed eccentrically between the oil and the envelope, and in the younger cells the envelope is lined by a layer of protoplasm. The envelope, indeed, is a periplast that is either secreted by the protoplasm, or is a transformation of it. When the cell becomes fully formed, the protoplasm may in some cases entirely disappear, but most commonly a portion of it remains, and extends like a ring from the nucleus around the cell (Fig. 80). The nucleus and protoplasm may be stained with carmine. The envelope may be seen as a thin clear band after the fat has been blackened with osmic acid (Fig. 81, *c*). It is, however, more apparent after the fat has been abstracted from the cells by washing them with ether; but it is rendered most evident by injecting a dilute solution of silver nitrate (1 : 1000) into the subcutaneous tissue of such an animal as a rabbit immediately after death. Shortly after the injection it is found that the envelope is separated from the fat by a considerable interval filled with a colourless fluid (Ranvier, *Op.* 39, p. 344).

The fat chiefly consists of palmitin and olein, with stearin in much smaller amount. When the body cools at death, the palmitin and stearin often form colourless acicular crystals, that have been termed "margarin" crystals, from an erroneous idea as to their nature. These crystals nearly always appear in fat cells when preserved in glycerin. The pale yellow colour of a fat cell is due to a peculiar pigment, which is soluble in the fat. It remains behind in the form of yellowish granules, when the fat disappears in emaciation (Toldt, *Op.* 65, p. 74).

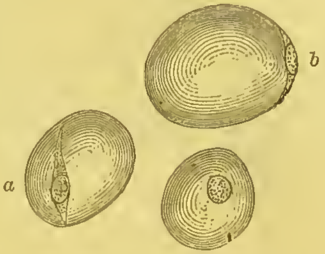

Fig. 80. Fat cells drawn after carmine-staining. A nucleated band of protoplasm is seen superficially in *a*, and in profile in *b*. In *c* there is a nucleus without protoplasm. × 300.

In ordinary areolar tissue, fat cells are commonly arranged in clusters in the form of islands or cords, that are mostly surrounded by a sheath of connective tissue, which may send in fine processes here and there between the cells; usually, however, the cells have scarcely anything save capillaries between them. The capillaries form a close network with the fat cells in the intervals, so that the interchange of material between the blood and the cells may be facilitated.

Toldt (*Op.* 65, p. 180) states that he has found lymphatics and nerves amidst fat cells. Flemming, however (*Op.* 18, xii. p. 500), denies the existence of lymphatics, and maintains that there is no evidence that the nerves are distributed to anything more than the blood-vessels.

Effect of Starvation.—In emaciation, the fat entirely disappears from adipose tissue in most situations, leaving the envelopes of the cells somewhat collapsed. The nucleus and protoplasm remain, while the fat is to some extent replaced by a clear fluid. Such cells have consequently been termed *serous* fat cells. The fluid, however, differs from serum, inasmuch as acetic acid occasions a precipitate—probably of mucin (Toldt, *Op.* 65, p. 72). As already stated, the pigment of the fat does not appear to be absorbed from the cells. In cases of prolonged emaciation, Flemming (*Op. cit.* p. 501) has pointed out that many of the capillaries of the adipose tissue become atrophied and disappear.

Effect of Irritation.—In emaciation, the nucleus of the fat cell sometimes proliferates, so that a group of young cells appears within the envelope of the parent. When fat cells are irritated by the injection of such a substance as a solution of iodine into the subcutaneous tissue of a living animal, the nucleated protoplast of the cell multiplies, and a brood of young cells thus appears between the fat and the envelope (Czajewicz, *Op.* 15, year 1866, p. 289).

DEVELOPMENT.—In skin, intermuscular fascia, and loose connective tissue generally, fat cells are, as Rollett (*Op.* 38, i. 95) and Toldt (*Op.* 65, p. 71) correctly maintain, mostly developed from rounded finely granular cells (Fig. 81, *a*). These fat-forming cells are usually numerous at the spot where the formation of adipose tissue is taking place. They multiply by cleavage (Fig. 81, *a′*), and appear in the first instance to be the descendants of connective tissue cells. In marrow, fat cells are developed from the medullary cells (Fig. 74, *e*). The fat appears at first as fine globules amidst the protoplasm that eventually coalesce and cause the protoplasm and nucleus to occupy an eccentric position, as already stated. The protoplasm at first forms a continuous layer around the fat, but it in time largely disappears. Flemming (*Op.* 18, xii. p. 500) states that fat cells arise directly from branched connective tissue corpuscles, but although such a mode of development doubtless occurs (Fig. 81, *d*), it is to be regarded as exceptional. Adipose tissue is mostly developed in the vicinity of blood-vessels, and its remarkable vascularity is due to growth of new vessels, either as buds from those already existing, or from the transformation of connective tissue corpuscles in the manner already indicated (p. 62).

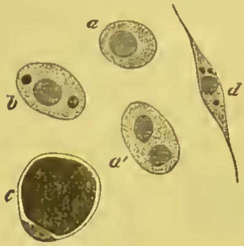

Fig. 81. Development of fat cells in omentum of guinea pig. *a*, Young fat cell; *a′*, with divided nucleus; *b*, fat appearing in the cell; *c*, fully formed fat cell; *d*, connective tissue corpuscle becoming a fat cell. Stained with osmic acid. × 350.

FUNCTIONS.—Adipose tissue discharges several important functions. 1. It forms a soft but elastic cushion in the orbit, on which the eyeball rotates. In the skin it gives softness and diffuses pressure, hence it is largely developed in the sole of the foot, in the gluteal region, and in some other parts. 2. It retards the radiation of heat from the cutaneous surface. On this account it is developed to a very remarkable extent in the skin of the whale. 3. It discharges an important function in nutrition, inasmuch as it secretes fat, and stores it up for the needs of the economy. The question as to the source of the fat in adipose tissue must be considered under the subject of *Nutrition*, of which it is an important problem. It may, however, be briefly stated here that there is sufficient reason for supposing that, just as the cells of the liver have the power of producing *glycogen* from sugar and proteids, and of storing it up within them for a time, in like manner the protoplasm of fat cells seems to have the power of producing *fat* from amyloids, and also from proteids, and the secretion is stored up in the cells until required. It may, however, also be that when an excess of fat is introduced into the blood from the food, a part of it is abstracted and accumulated in the fat cells. But experimental evidence will afterwards be adduced to show that this probably takes place to a less extent than is commonly supposed. When the fat is absorbed from the fat cells into the blood, it is not known whether it passes from the cell unchanged, or is converted into soluble soaps to facilitate its removal. The circumstance—already mentioned—that the yellow pigment of the fat is left behind favours the latter idea (Toldt, *Op.* 65, p. 74).

CHAPTER X.

THE TEETH.

General Characters.—In the human subject there are two sets of teeth:—1. The *temporary*, *deciduous*, or *milk* teeth. 2. The *permanent* teeth. Their several numbers and names are indicated in the following formulæ:—

		Molar.	Canine.	Incisor.		Canine.	Molar.	
Temporary	Upper,	2	1	2	2	1	2	= 20
	Lower,	2	1	2	2	1	2	

		Molar.	Bicuspid.	Canine.	Incisor.		Caninc.	Bicuspid.	Molar.	
Permanent	Upper,	3	2	1	2	2	1	2	3	=32
	Lower,	3	2	1	2	2	1	2	3	

The teeth are fixed in sockets (alveoli) in the maxillary bones. The imbedded part of a tooth is termed the *fang*, its free portion—the crown, and the somewhat constricted line of junction between the two—the *neck*. The general characters of the permanent teeth are as follows:—The chisel-shaped crown of the incisors and the pointed crown of the canine teeth are both of them adapted for cutting and tearing the food; but in carnivorous animals the crown of the canine teeth is greatly elongated, and serves as a weapon. The crowns of the bicuspids and molars are comparatively broad and adapted for grinding. There is a single fang in the incisors and canines. The fang of the bicuspids is sometimes single, sometimes double. The molars of the lower jaw have two, those of the upper jaw have three fangs; but in the wisdom teeth the fangs are usually more or less compressed together. The presence of more than one fang in the molar teeth is probably of service in keeping them steady during lateral strain to which their crowns are subjected in the act of grinding the food.

Structure of the Teeth.

All the teeth, whether temporary or permanent, have essentially the same structure, each tooth consisting of four parts: the *pulp*, filling a central space—the pulp cavity (Fig. 82, *p*); the *dentine* (*d*), surrounding the pulp cavity; the *enamel* (*e*), covering the dentine in the crown; and the *cement* (*c*), covering it in the fang. Excepting the pulp, all these parts are exceedingly hard. Blood-vessels and nerves enter the pulp through an aperture at the point of the fang.

The Cement, or Crusta Petrosa, is a thin plate of bone enclosing the dentine of the fang. It (*c*) consists of bone-corpuscles in lacunæ, with canaliculi embedded in a matrix composed of calcified fibrous tissue arranged in lamellæ. Many fibres of Sharpey pierce the lamellæ from the surrounding periosteum—or, as it is here named, periodontal membrane—and are probably of service in fixing the tooth in the alveolus.

THE ENAMEL covers the dentine in the crown of the tooth. It is thickest over the upper part of the crown, and gradually thins off towards the neck, where it is overlapped to a slight extent by the cement. The outer surface of the enamel is finely striated transversely to the long axis of the tooth. Sometimes there are a few deep grooves, due to imperfect development of the tooth. Enamel is the hardest tissue in the body, and consists almost entirely of earthy salts, chiefly calcium phosphate, with only from 3 to 5 per cent of organic matter. On this account it is almost entirely dissolved by dilute mineral acids. It is composed of solid prisms or fibres, from 3 to 4 μ in breadth. The prisms are set endwise on the dentine (Fig. 83), and are in close apposition, there being scarcely any interstitial matter between them. Sometimes, however, there are irregular fissures between their inner ends (*f*). The fibres run in bundles, which often decussate at their inner extremities. In transverse section the fibres may be hexagonal, but often they are polygonal (T). The prisms may be isolated by placing a thin vertical section of enamel—parallel with the fibres—for a short time in dilute hydrochloric acid, and then dissecting it with needles, and subjecting the fragments to pressure. Each fibre has a somewhat wavy outline, and is marked at tolerably regular intervals by fine clear transverse lines. Hertz ascribes these to intermittent calcification of the fibres, an explanation that receives support from the circumstance that the lines become more evident after the action of dilute mineral acid, and also from the fact that transverse cleavage of the fibre through these clear lines may be effected by mechanical pressure after the acid has acted for some time.

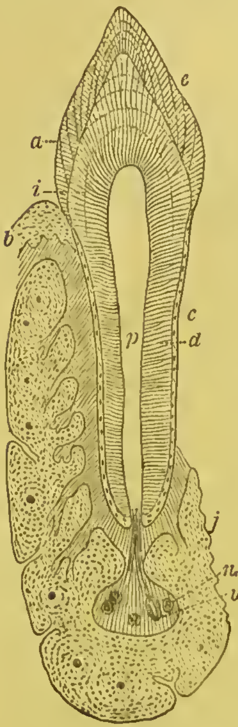

Fig. 82. Vertical section of a cat's tooth, with part of the alveolus and lower jaw (*j*). *p*, Pulp cavity; *d*, dentine; *c*, cement; *e*, enamel; *a*, coloured striæ in enamel; *i*, incremental lines in dentine; *b*, epithelium of gum; *n*, nerve; *v*, blood-vessel cut across in the dental canal. (*Semidiagrammatic.*)

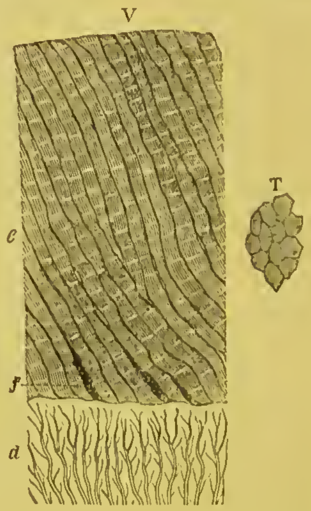

Fig. 83. V, Vertical, T, transverse section of enamel fibres (*e*); *f*, fissure between the fibres; *d*, dentine. × 300.

In a vertical section of a tooth, coloured lines, the *brown lines of Retzius*, may be seen crossing the enamel fibres and forming a series of arches more or less complete (Fig. 82, *a*). They are in much smaller number than the fine colourless lines just described. Von Bibra has chemically examined the pigment in the beaver and squirrel, and finds it to be oxide of iron. Kölliker ascribes the concentric arrangement of the coloured lines to a laminated mode of formation of the enamel.

Nasmyth's membrane, or the *cuticle of the enamel*, is a thin calcified membrane covering the enamel in the young subject. It is but little affected by hydrochloric acid. It swells up in caustic potash, and when burned emits an odour of burning horn. Waldeyer therefore supposes it to be of a horny nature, and to consist of calcified epithelial cells (*Op.* 38, i. 474), and he states that their outlines may be revealed by the silver process. According to J. Tomes, however, Nasmyth's membrane is a thin layer of crusta petrosa without lacunæ (see p. 119). Nasmyth's membrane is soon worn away by friction, and eventually, as age advances, the enamel fibres are themselves worn away, and the dentine exposed.

THE DENTINE OR IVORY constitutes the greater part of the tooth. It consists of tubules imbedded in a calcified matrix, chemically like that of bone, but structurally different, inasmuch as the organic part is not fibrous, but homogeneous. The *dentinal tubules* open into the pulp-cavity, radiate through the dentine, and end near its periphery. Sometimes, however, they open into the fissures in the enamel, or run between its fibres for a short distance; or they may communicate with the canaliculi in the cement (Tomes). In their course through the dentine they are wavy, having two or three primary, and a large number of secondary curvatures (Fig. 84, *d*). They divide once or twice dichotomously, and each primary branch gives off a large number of minute secondary branches, many of which form loop-like anastomoses with those of neighbouring tubules. The cavity of the tubules is largest (5 to 6 μ) near the pulp-cavity, and diminishes outwards. The walls of the tubules, the *dentinal sheaths,* consist of a homogeneous yellowish membrane, that probably consists of elastin, seeing that it is scarcely affected by boiling in strong mineral acids or caustic alkali. As the intertubular matrix is entirely destroyed by such treatment, the dentinal tubules may be isolated thereby.

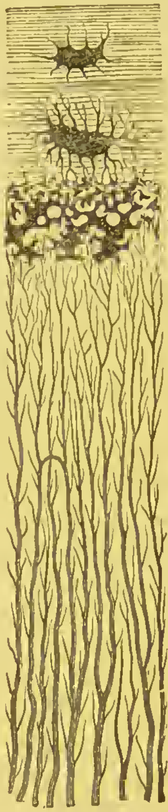

Fig. 84. Transverse section of fang of human tooth. *d*, Dentinal tubules; *i*, interglobular substance; *c*, cement. × 300. (Waldeyer.)

Dentinal Fibres.—Each tubule contains a fine fibre—the *dentinal fibre*, or *fibre of Tomes* (Fig. 85, *f*). In a thin transverse section of the tubules of decalcified dentine, the fibre appears as a minute dark spot enclosed by a thin yellowish ring—the dentinal sheath. The dentinal fibres are processes of cells—the *odontoblasts* that lie in the pulp-cavity close to the dentine. Sometimes, in sections of softened teeth, the odontoblasts are partially dislocated, and the dentinal fibres may be seen stretching like harp-strings between them and the dentine. Also, when unsoftened sections of recent dentine are broken across, the fibres may be seen extending between the fragments. When over-stretched they break, and a sort of bead often forms at the broken end (J. Tomes), indicating that the fibres are in their normal condition soft and colloid. They may be

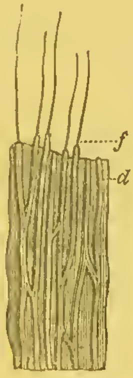

Fig. 85. *d*, Dentine torn across, showing the dentinal tubules and fibres projecting (*f*). From incisor tooth of rabbit, after maceration for several weeks in "strong" chromic acid solution. (Boll.)

stained with carmine, though with difficulty (C. S. Tomes). They probably traverse the whole extent of the dentinal tubules and their divisions, but, owing to the difficulty of the case, they have not been traced into the finest branches. In old age they atrophy or become calcified.

Interglobular substance.—The outer part of the dentine, especially in the fang, presents a granular appearance when an unsoftened section of tooth is examined with a low magnifying power. This—the *granular layer* of J. Tomes—is, when highly magnified, seen to consist of "interglobular spaces," so called because in sections of dried tooth they appear as cavities with the calcified dentine projecting into them in a globular form. Normally, however, they are not spaces (Waldeyer), but are filled with a soft matter, apparently dentine that has escaped calcification (C. S. Tomes, *Op.* 59, p. 64).

Curved lines in the dentine.—The matrix of the dentine is laminated. The outlines of the laminæ run at right angles to the dentinal tubules, and are concentric with the pulp-cavity (Sharpey). They may be readily seen in a transverse section of the fang of an unsoftened tooth, which, after decalcification, splits into concentric rings (Salter). As they indicate a laminated formation of the dentine during its growth at the surface of the pulp-cavity, they are termed incremental lines. They are also visible in a vertical section of a tooth, and it occasionally happens that some of these incremental lines are in the crown of the tooth—rendered more conspicuous by imperfect calcification of the dentine. These are the "contour lines" of Owen (Fig. 82, *i*). When highly magnified they are seen to be due to lines of interglobular substance.

Schreger pointed out that in a vertical section of unsoftened tooth the primary curvatures of the dentinal tubules give rise to two or three faint lines concentric with the pulp-cavity. These have consequently been named "Schreger's lines."

The Pulp consists of a delicate connective tissue containing numerous cells, vessels, and nerves. Close to the dentine there is a layer of relatively large nucleated cells, the *odontoblasts* (Fig. 89, *o*), that are to be regarded as modified connective tissue corpuscles. These cells have fine processes that may be grouped in three sets,—external, lateral, and central (Waldeyer, *Op. cit.*) The *external* processes are the dentinal fibres, of which one, two, or three may spring from a single odontoblast. The *lateral* processes connect neighbouring odontoblasts, while the *central* ones join them to connective tissue corpuscles situated more centrally in the pulp. The nerves of the teeth are derived from the fifth cranial nerve. They form a rich plexus in the pulp. Boll (*Op.* 18, year 1868, p. 75) has traced the nerve fibrils to the dentinal tubules, but whether they enter the tubules and traverse them along with the dentinal fibres, or join the dentinal fibres, is unknown. It cannot be doubted that a sensitive tissue of some sort extends throughout the dentine, for when caries attacks its outer part it becomes exceedingly sensitive, and on the removal of the carious portion, it is found that the normal dentine, although nearer the pulp-cavity, is far less sensitive (C. S. Tomes, *Op.* 59, p. 72).

The Alveolo-dental Membrane (periodontal membrane) is the periosteum intervening between the fang and the alveolar wall. It contains numerous blood-vessels and nerves. Many perforating fibres pass from it into the crusta petrosa.

The enamel of the teeth is gradually worn away by friction, and it is liable to suffer disintegration from other causes, chief among which are probably the micrococci and bacteria that nestle in the sordes. Hence the importance of their daily removal. Wood charcoal is the best dentifrice (Christison).

Development of the Teeth.

Development of the Temporary Teeth.—The teeth are developed in the mucous membrane of the maxillary ridges, the enamel being formed from its epithelium and the remaining dental tissues from the sub-epithelial connective tissue. The portions of the epitheliated surface and the subjacent connective tissue concerned in the development of a tooth together constitute the *dental germ.*

About the seventh week of fœtal life, the epithelium covering the border of the maxillary ridge grows thicker, and forms two slight longitudinal ridges—the *dental ridges*—with a shallow groove between them, which may be termed the *superficial dental groove.* A transverse section of the maxillary ridge shows that this groove is merely a depression on the surface of the oral epithelium, due to an active growth of the cells at its margins. It, however, broadly marks the position of what may be termed the *deep dental groove*[1] (Fig. 86, *d*), formed by a downward growth of the deeper portion of the epithelium into the soft mucous connective tissue. The deep dental groove extends throughout the whole length of the jaw, and the epithelium with which it is filled is termed the *common enamel germ.* Flask-like dilatations make their appearance at intervals in the deep dental groove, owing to rapid epithelial proliferation at certain points. Each dilatation marks the site of a future temporary tooth, and the epithelium which fills it is termed the *special enamel germ*, or *enamel organ.*

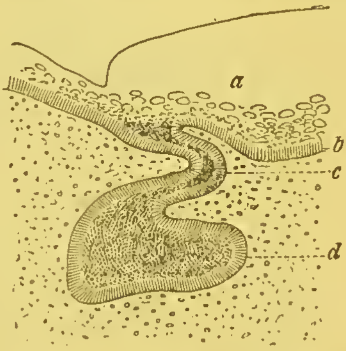

Fig. 86. Traverse section of the maxillary ridge of a ruminant, showing the early condition of the dental follicle. *a*, Superficial; *b*, deep layer of oral epithelium; *c*, deep dental groove; *d*, dilated portion containing the special enamel germ. (Kölliker.)

A papilla—the *dentine germ*—grows upwards at the base of the enamel organ, and indents it (Fig. 87, *g*). Consisting of mucous connective tissue in which blood-vessels soon appear, it eventually becomes the dentine and the tooth pulp. Inferiorly, it is continuous with the vascular connective tissue that envelops the enamel organ, and which becomes the dental sac (*s*), in whose interior the tooth is developed. The terms *follicular* and *saccular* were applied by Goodsir to the stages of tooth-development before and after the formation of the dental sac.

Owing to the secondary dental groove in most cases bending inwards as it deepens, the narrow fissure (*e*), by which the enamel organ communicates with the oral epithelium usually acquires a lateral position with reference to the tooth sac. It eventually becomes obliterated (Waldeyer,

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[1] Goodsir (*Op.* 7, year 1838, and *Op.* 50, ii.), to whom we owe many important facts regarding the development of the teeth, designated the *superficial* and *deep* dental grooves "*primitive*" and "*secondary*;" but as the imperfect histological methods at his disposal in 1838 led him into error regarding the development and significance of these grooves (which were first indicated by Kölliker, *Op.* 53, year 1863), it is thought advisable to adopt the nomenclature of the text.

Op. 38, i. 483), so that, even when it happens to be placed over the centre of the tooth sac, the growing tooth emerges from the dental sac by pressing against the superjacent tissues of the gum, until they are absorbed.

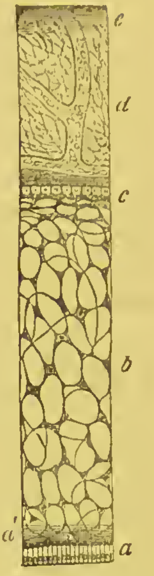

Fig. 88. Vertical section of enamel organ and dental sac of child, at birth (Kölliker). *a*, Inner layer with *stratum intermedium* external to it; *b*, gelatinous layer; *c*, outer layer of enamel organ; *d*, loose fibro-vascular (inner) layer; *e*, dense fibrous (outer) layer of dental sac. × 250; reduced one half.

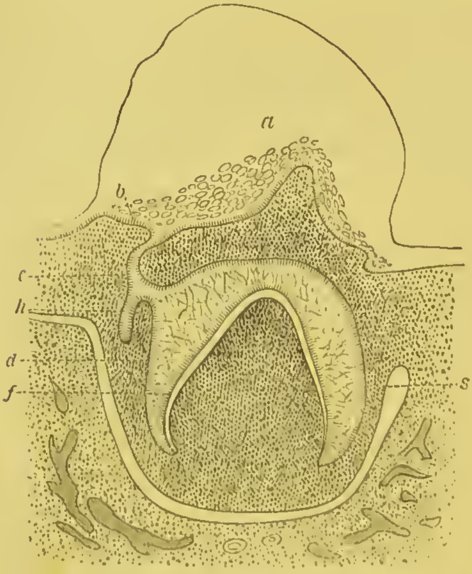

Fig. 87. A more advanced stage in the development of the tooth of a ruminant. *a*, Superficial; *b*, deep layers of oral epithelium; *c*, neck of the deep dental groove; *d, e, f*, outer, middle, and inner layers of cells of enamel organ; *g*, dentine germ; *s*, the commencement of the dental sac; *h*, formation of a special enamel germ for a permanent tooth. (Kölliker.)

Formation of the Enamel.—The enamel organ forms a cap-like covering to the dentine germ. It at first consists of tolerably uniform epithelial cells, but ere long it differentiates into four layers: the external epithelium (Fig. 88, *c*); the enamel pulp (*b*); the stratum intermedium a'; and the internal epithelium (*a*). 1. The *external epithelium* consists of a row of cubical or low columnar cells lining the dental sac. These are continued into the cells of the inner layer at the base of the dental papilla. 2. The *enamel pulp* resembles mucous tissue, in so far as it is a meshwork of stellate cells with anastomosing processes, and a jelly-like fluid filling their interstices. The fluid is of an albuminous nature, and the cells are undoubtedly of epithelial origin. 3. The *stratum intermedium* is composed of two or three layers of somewhat rounded cells that appear to be undifferentiated cells of the enamel germ. 4. The *internal epithelium* consists of a single layer of hexagonal columnar cells—the *enamel cells*—that become transformed into the enamel prisms. Each cell has a nucleus near its outer extremity. Calcification begins at its inner end, and first involves the periphery of the prism, so that, if the enamel cells be forcibly detached, a pointed prolongation of the axial part of the cell ("Tomes' process") may be pulled from the centre of each prism (Fig. 89, *g*). The nucleus of the cell disappears, and the enamel prism is therefore to be regarded simply as a periplast.

Waldeyer states that many of the cells of the stratum intermedium become transformed into enamel cells. The enamel pulp takes no part in the formation of the tooth; as development proceeds it entirely disappears, so that the external epithelium comes to be in contact with what remains of the stratum intermedium (Fig. 89, c', c''). The latter disappears, and, according to Waldeyer (*Op.* 38, i. 485) and Hertz (quoted by Waldeyer, *Op. cit.*), the external epithelial cells become cornified, and constitute Nasmyth's membrane. But, on the other hand, C. S. Tomes (*Op.* 59, p. 94) adduces evidence in support of the view originally advanced by J. Tomes, that Nasmyth's membrane is a thin layer of coronal cement, strictly homologous with the thick coronal cement of herbivora. It is continuous with the outer part of the cement in the fang, and, like it, is developed from osteoblasts derived from the dental sac. On this view he explains the occasional presence of bone-corpuscles in Nasmyth's membrane, especially in fissures in the enamel. He supposes that in most instances the bone-corpuscles entirely disappear in the process of calcification, and that the silver outlines seen by Waldeyer in Nasmyth's membrane (p. 115) are the outlines, not of the epithelial cells, but of cell-territories of the previously existing bone-corpuscles. With reference to the general absence of lacunæ from the membrane, he states that the thinnest layers of unquestionable cement are also without lacunæ. Further, in this connection, Magitot (quoted by Tomes, *Op. cit.*) is of opinion that the external epithelium of the enamel organ entirely disappears before the development of the enamel prisms is completed.

Formation of the Dentine and Pulp.—The dentine germ at first consists of mucous tissue, with numerous capillaries. Its outer cells become transformed into a layer of odontoblasts, whose peripheral processes become the dentinal fibres, and the dentinal matrix is formed between them immediately external to the odontoblasts. As the dentine grows thicker, the dentinal fibres elongate, and the odontoblasts recede from the periphery.

Whether or not the dentinal matrix is a secretion from or a direct conversion of the odontoblasts, is a disputed point. Waldeyer (*Op.* 38, i. 489) holds that the dentine is formed by the direct conversion of several successive layers of odontoblasts, their central parts remaining as the dentinal fibres, while their peripheral parts are transformed into the dentinal sheaths and matrix. But although the formation of enamel prisms tempts the mind to entertain the *conversion theory*, we have failed to see any evidence of it in the dentine, and cannot but think it highly probable that the dentinal matrix, at all events, is not formed in this manner, but—like the matrix of cartilage (p. 77), and doubtless also that of bone—it is probably a secretion from the odontoblasts.

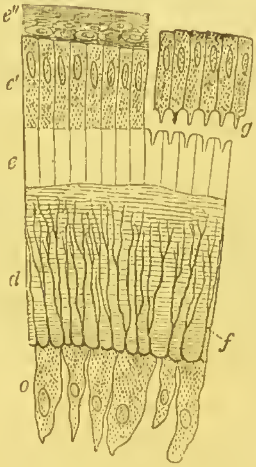

Fig. 89. Vertical section of growing enamel and dentine from young decalcified tooth of rabbit. *e*, Enamel prisms ; *e'*, enamel cells *in situ*, but detached at *g*, and showing Tomes' processes ; *e''*, cells of external layer and stratum intermedium of enamel organ ; *o*, odontoblasts ; *f*, dentinal fibres ; *d*, matrix. × 1200.

The matrix (Fig. 89, *d*) is collagenous like that of bone, and is at first uncalcified, but after a time calcification occurs at the periphery and extends inwards. The calcification begins at separate points that assume a globular shape, and, as they grow larger, coalesce. But if the calcification is arrested before coalescence ensues, *interglobular spaces* are the result. It would be difficult to say whether the dentinal sheaths are a transformation of the matrix or a conversion of the periphery of the dentinal fibres. The central part of the dentine germ remains as the tooth pulp.

The *cement* is formed by ossification of the inner and lower part of the fibrous tissue of the dental sac, the outer part of which becomes the *alveolo-dental membrane.* It has been already stated that, in the opinion of Tomes, the inner part of the dental sac that covers the enamel is converted into Nasymth's membrane. The bone of the jaw grows in the connective tissue at the periphery of the dental sacs, and in this manner the alveoli are formed.

ERUPTION OF THE TEMPORARY TEETH.—The eruption of a tooth is due to the elongation of its fang, which raises the crown above the level of the jaw and gum, and causes it to cut its way by absorption through the latter. The local irritation set up by the process is occasionally the cause of a general systemic disturbance, so serious that it is sometimes necessary to facilitate the process of eruption by incising the gum over the emerging tooth. It is, therefore, particularly important in practical medicine to remember the periods at which the temporary teeth severally emerge. Their eruption begins at the age of *seven* months, and the teeth that appear first are the central incisors of the lower jaw. These are quickly followed by the central incisors of the upper jaw; and, in like manner, the rest of the upper teeth emerge immediately after the corresponding teeth of the lower jaw, and the teeth on both sides of the jaw appear simultaneously. The following table indicates the *months* at which the temporary teeth emerge:—

Incisors.	Canines.	Molars.
7, 9	18	12, 24

DEVELOPMENT AND ERUPTION OF THE PERMANENT TEETH.—Although the first tooth of the permanent set (the front molar of lower jaw) does not emerge until the sixth year, the development of all the permanent teeth, excepting the two last molars, begins at an early period of embryonic life. The incisors, canines, and bicuspids of the permanent set are severally developed behind the corresponding milk-teeth, in follicles—termed by Goodsir *cavities of reserve*—that are developed from an involution of the common enamel germ at the neck of the follicles of the milk-teeth (Fig. 87, *h*). This secondary follicle becomes pear-shaped, and a solid pedicle unites it to the gum at the neck of the milk-tooth (Fig. 90, *c*). The permanent tooth grows inside its follicle in a manner precisely similar to that of the milk-tooth. Its sac becomes separated from the socket of the latter by the growth of the bony wall of the alveolus (Fig. 90); but as the permanent tooth elongates and presses upwards, it causes absorption of the intervening part of the alveolar wall, and grows into the socket of the milk-tooth. The process is facilitated by the absorption of the fangs of the milk-teeth, through the agency of cells, as J. Tomes first pointed out. The cells are *osteoclasts*, or, as they may be termed in this connection, *odontoclasts*, that make their appearance on the surface of the fang in the alveolo-dental membrane. The first (anterior) molar of the permanent set begins to grow from the deep dental groove—in the same manner as a milk-tooth—about the sixteenth week of embryo-life. According to Magitot and Legros (*Op.* 12,

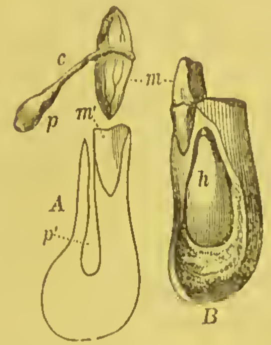

Fig. 90. *A*, Milk-tooth (*m*), with sac (*p*) and pedicle (*c*) of permanent tooth detached from their bony recesses (*m'* and *p'*) in a transverse section of the lower jaw at an early period after the eruption of the milk-teeth. *B*, Section of the jaw shortly before the eruption of the permanent tooth (*h*). *B* is of the natural size; *A* is somewhat enlarged (Blake.)

year 1873), the second permanent molar begins to grow about the third month after birth, in a cavity developed from the neck of the follicle of the first permanent molar; and the wisdom tooth, in like manner, grows in a cavity developed from the follicle of the second molar, which does not appear, however, until so late as the third year. The following table indicates the *years* at which the permanent teeth emerge:—[1]

Incisors.	Canines.	Bicuspids.	Molars.
7, 8	11 to 12	9, 10	6, 12 to 13, 17 to 25

CHAPTER XI.

CONTRACTILE TISSUES.

THE contractile tissues are those which give rise to ordinary mechanical motion by undergoing forcible changes of shape. The direction of their movement may be *indefinite* or *definite.* Motion in an *indefinite* direction is produced by the amœboid cells already studied, viz. blood and lymph leucocytes, mucus corpuscles, and the wandering cells of connective tissue. Muscle, cilia, and certain pigment cells, give rise to motion in a *definite* direction. As ciliary movement has been already studied (p. 71), this chapter will be devoted to contractile pigment cells and muscle.

CONTRACTILE PIGMENT CELLS.

Although contractile pigment cells are foreign to human physiology, they are of such physiological interest that they must be considered here. They occur largely in the skin, around the visceral blood-vessels of the frog, cameleon, and some other allied vertebrates, and they may be readily studied in the frog's web. They are modified connective tissue corpuscles, which they resemble in their flattened shape and branched appearance; their processes anastomose with one another, and with those of neighbouring cells (Fig. 91). Each cell is nucleated, and the cell substance contains granules of pigment of a dark brown colour in the frog, which is apparently melanin. The cells are under the influence of motor nerves, which, when excited, induce their contraction. In what may be termed the relaxed state of the cell, the pigment granules are diffused throughout the cell generally, while in the state of contraction they are partially or completely concentrated in its central part (Fig. 92), the general configuration of the cell-space remaining unchanged (Lister, *Op.* 3, year 1858). The skin of the frog is pale when the pigment is concentrated, dark when diffused. In the tree-frog (*Hyla arborea*) Wittich (*Op.* 14, year 1854) found that the cells contract when the skin is irritated mechanically by turpentine, or by electricity; when the nerves of the part or the spinal cord are excited by electricity; and when the animal is exposed to light. On removal of the stimulus, diffusion of the pigment ensues. He ascertained that the esculent frog (*Rana esculenta*) is far less sensitive to local irritation; and Lister (*Op. cit.*) found that, in the ordinary English frog (*Rana temporaria*) the cells are little influenced by local irritation, while they are readily affected by direct irritation of their nerves, or by the influence of light. When the nerves of a frog's leg are divided its pigment cells relax, and remain in this condition as long as the circulation continues, but on its cessation they become contracted; a condition that is probably analogous to the rigor mortis of muscle. On exposing a frog, with one sciatic nerve divided, to a bright light, the paralysed limb remains dark while the rest of the body becomes pale; showing that the cells are excited by light—not directly, but through their nerves. Lister found that after removal of the frog's eyeballs a bright light was no longer able to render the skin pale; showing that the light excites the pigment cells through an indirect (*reflex*) nervous mechanism consisting of a peripheral nerve termination—the retina—stimulated by the light; an efferent nerve—the optic—to convey the excitement to a nerve-centre in the brain; and efferent nerve-fibres—contained in the medulla, spinal cord, and cerebrospinal nerves—to convey it to the pigment cells. The cells often contract when the animal moves; probably in that case their movement is due to emotional excitement.

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[1] For a more detailed account of the teeth, the excellent work by C. S. Tomes (*Op.* 59) and the chapter on the Teeth by Waldeyer in *Op.* 38, may be consulted with advantage. In both, the literature of the subject is fully given.

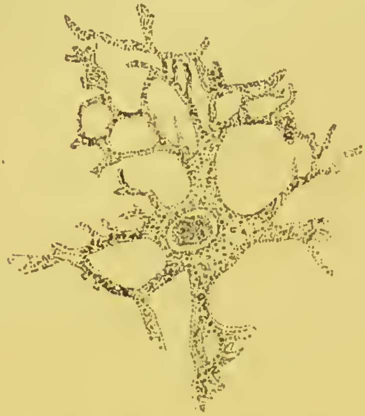

Fig. 91. Pigment cell relaxed. From frog's web. × 500. (Lister.)

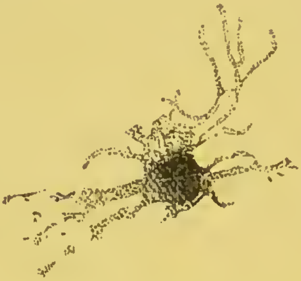

Fig. 92. Pigment cell partially contracted. × 250. (Lister.)

The concentration of the pigment granules was ascribed by Wittich (*Op. cit.*) and others to contraction of the processes of the cell protoplasm, but Lister (*Op. cit.*) opposes this idea because there is no bulging in the centre of the contracted cell, and also because a clear fluid is left in the branches of the cell space. It is to be remembered, however, that when the protoplast of a cartilage cell shrinks and gathers around its nucleus (Fig. 39, *c*) fluid is expressed from the interstices of the protoplasm, and fills the periphery of the cell space. To refer the movements of the pigment granules to their carriage to and fro in hyaline protoplasm after the fashion of granules in the pseudopodia of an amœba is most in harmony with our knowledge of other contractile movements, and it is difficult to believe with Lister that the pigment granules alone move to and fro. The point, however, requires further investigation, and the anatomical relations of the nerves to the cells also require elucidation.

MUSCULAR TISSUE.

Muscular tissue is the mainspring of most of the mechanical work of the organism. It consists of cells that are nearly always in the form of fibres. The protoplasm of each cell is differentiated into fine fibrils that are *contractile* and *elastic*. Their contraction consists in a forcible shortening, accompanied by an increase of thickness. The work they perform is, however, always immediately referable to their *shortening* and not to their thickening. There are two varieties of muscular fibres, the striped and the unstriped. The latter being the simpler of the two will be studied first.

UNSTRIPED MUSCLE.

Unstriped, non-striated, or organic muscular fibre, is found in the alimentary canal below the middle of the œsophagus; in the trachea and bronchi; in arteries, veins, and lymphatics; in the bladder, ureters, urethra, and in the male and female genital organs. It is also found in the skin, iris, ciliary muscle, and in some other parts. In the pharynx, upper half of the gullet, and heart, the muscular fibre is *striped;* apparently because more rapid contraction is needed in these parts of the hollow viscera: the contraction of striped muscle being more rapid than that of unstriped. As the action of non-striped muscle is, in most instances, involuntary, it is sometimes so designated. But the term involuntary is misleading, for while the heart—an *involuntary* muscle—is composed of *striped* fibres, the urinary bladder, which *mostly acts under the influence of volition*, consists of fibres that are *unstriped.*

Structure and Arrangement of the Fibres.

The fibres, though sometimes occurring singly, are for the most part arranged in groups, constituting laminæ—as in the blood-vessels; or distinct fasciculi—as in the bladder. The fibres overlap at their ends, and are within a fasciculus held together by a connective substance named the *perimysium internum* or *endomysium*, consisting of a homogeneous albuminous matrix containing branched cells (Fig. 93, *p*). The fasciculi are enveloped in ordinary connective tissue (the *perimysium externum*).

The fibres of unstriped muscle may be readily examined in certain thin membranes, such as the bladder of the frog and salamander, the mesentery of the newt, and in small blood-vessels. The fibres are mostly fusiform, with their ends undivided and tapering to slender points (Fig. 93, *a*, *a'*); but sometimes, especially in the urinary bladder and blood-vessels, their ends are branched. In the frog's bladder the fibres are often triradiate, and in that of the salamander they may have as many as five or six processes. Their transverse sections are mostly elliptical, sometimes cylindrical, but—in unhardened fibres—rarely polygonal. In breadth they vary from 4 to 10 μ ($\frac{1}{6000}$ to $\frac{1}{2500}$ inch) in length—from 40 to 200 μ ($\frac{1}{600}$ to $\frac{1}{120}$ inch), but in the pregnant uterus they are considerably longer ($\frac{1}{40}$ inch). They are colourless and transparent, and their general substance has for the most part a homogeneous aspect, unless after treatment with certain reagents, when it exhibits a longitudinal fibrillation. This, however, as Wagener (quoted by Arnold, *Op.* 38, i. 191) first pointed out, is sometimes dimly visible near the ends of the fibres in their *fresh* condition. But the fibrillation becomes evident throughout the whole length of the fibres when they are placed for twenty-four hours in a solution of ammonium chromate (five per cent), and afterwards stained with logwood or picrocarmine. The fibres of the bladder of the *Salamandra maculata*, as recommended by Flemming (*Op.* 18, xiii. 693), are especially suited for the demonstration of the fibrils. The mesentery of the newt is also available, and has enabled Klein (*Op.* 8, xviii. 328) to give an excellent description of the fibres. A fibre thus treated is seen to consist of an axial band of sarcous matter, composed of a bundle of excessively fine and apparently homogeneous fibrils (Fig. 94, *f*), enveloped in a sarcolemma (*m*). The sarcolemma of non-striped muscle (discovered by W. Krause, *Op.* 72, p. 99) is an extremely thin elastic membrane, with fine annular thickenings (Klein, *Op. cit.*) There is generally a single nucleus placed about the middle of the fibre. It is of oblong shape, has a membrane, and includes a delicate reticulum (Flemming, *Op. cit.*) According to Klein the fibrils are continuous with the intranuclear reticulum at the poles of the nucleus. Each fibre of non-striped muscle is therefore a cell, having a periplast (the sarcolemma) enclosing a nucleus, and protoplasm modified into contractile fibrils.

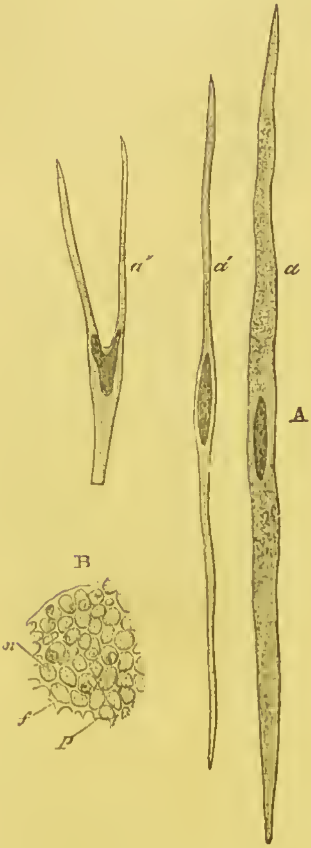

Fig. 93. Fibres of unstriped muscle. (A), Isolated after hardening in Müller's fluid; *a*, broad, *a'*, narrow fibre from wall of intestine; *a''*, triradiate fibre from frog's bladder. B, A fasciculus of fibres cut transversely after hardening in chromic acid; *f*, fibre; *n*, nucleus; *p*, endomysium. × 300.

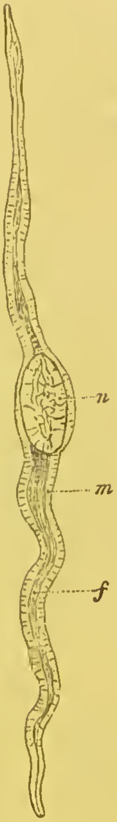

Fig. 94. Unstriped muscular fibre from mesentery of newt treated as stated in text. *n*, Nucleus; *f*, fibrils; *m*, sarcolemma. × 450. (Klein.)

The power of double refraction which the fibres possess will be alluded to under Striped Muscle.

STRIPED MUSCLE.

Striped, striated, or, as they are sometimes though improperly termed, voluntary muscular fibres, are the contractile elements in all the muscles of the trunk, diaphragm, heart, pharynx, and upper half of the œsophagus, in the sphincter of the bladder and external sphincter of the anus, and in the muscles of the outer and middle ear. The cardiac fibres, being in some respects peculiar, will be described separately.

Structure and Arrangement of the Fibres of Ordinary Striped Muscle.

The fibres of ordinary striped muscle are cylindrical, and taper to ends that are mostly undivided, but in the tongue, in the straight and oblique muscles of the eyeball, and in the facial muscles that are connected with the skin, the fibres are branched. The breadth of the fibres is least in the face, greatest in the limbs, and varies from 10 to 60 μ ($\frac{1}{2400}$ to $\frac{1}{400}$ inch). Their length varies from an inch and a half downwards.

STRUCTURE.—Each fibre is a modified cell having an envelope—the *sarcolemma*, enclosing several nuclei—the *muscle-corpuscles*, and a mass of soft contractile matter—the *sarcous substance.* The latter is a modification of the protoplasm of the embryonic cell, from which each fibre is developed.

THE SARCOLEMMA is a colourless, transparent, homogeneous, elastic membrane, chemically resembling elastic tissue. Although exceedingly thin, it is tough, and much less easily torn than the relatively thick cylinder of sarcous matter which it encloses (Fig. 95). It is connected by annular attachments with the sarcous substance at short intervals throughout the length of the fibre (Fig. 100, *s*).

THE NUCLEI or muscle-corpuscles are found immediately below the sarcolemma in mammals, but in the frog, water-beetle, and many other animals, they also occur in spaces amidst the sarcous substance (Fig. 101, *n′*). Those under the sarcolemma are flattened and oval, and occur irregularly throughout the length of the fibre (Fig. 101, *n*). Their presence is obscured by their being enveloped in a small quantity of undifferentiated protoplasm. But when this is rendered transparent by acetic acid, or when some staining agent is added, they are rendered evident.

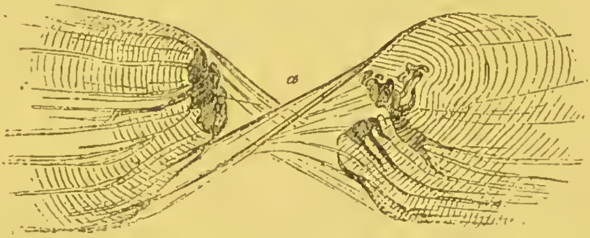

Fig. 95. Fragment of striped muscular fibre of skate, showing the sarcolemma (*a*) between the ends of the torn sarcous matter. (Bowman.)

THE SARCOUS SUBSTANCE has a somewhat complicated structure, which has been and is now the subject of no little controversy. The following account is therefore mainly confined to facts which we know to be capable of demonstration. The sarcous matter is crossed by a series of alternately *dim* and *clear stripes* or bands, which give a characteristic appearance to the fibres (Fig. 96). The stripes, although evident enough in vertebrate muscle, may be most advantageously studied in that of some invertebrates, because of the larger size of the morphological elements of which they are composed. The muscle of the common water-beetle

(*Dytiscus marginalis*) is specially suitable, because of the apparently close similarity in essential details between its structure (Fig. 96) and that of vertebrate muscle (Fig. 98). The muscle of another water-beetle—the *Hydrophilus piceus*, and that of the bee (Fig. 97), are also suitable.

Living fibres excised from the leg or wing muscles of the dytiscus, dissociated with needles, and examined at once, in their own juice, or in an aqueous solution of sodium salicylate (one per cent), with a power of 300 diam., readily show the alternate dim and clear transverse stripes. A fine dim line crosses the fibre in the middle of the clear stripe, and may with propriety be named Dobie's stripe after its discoverer (Fig. 97, *d'*). It is scarcely visible with a power of 300 diam., and can only be fairly studied with a power of at least 1200 diam. (Fig. 100, *d'*). The stripes are in no way due to the sarcolemma, but are confined to the sarcous substance, in which they are not superficial markings, but result from a special arrangement of its morphological elements throughout its whole thickness.

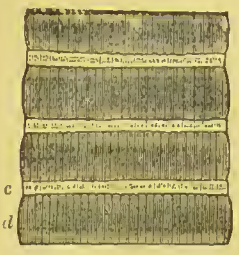

Fig. 96. Part of a fresh striped muscular fibre from the common water-beetle (*Dytiscus marginalis*). *d*, Dim stripe; *c*, clear stripe. × 800.

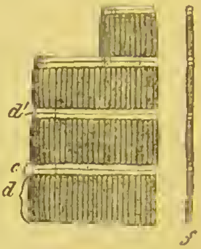

Fig. 97. Part of a striped muscular fibre of the bee after hardening in alcohol. *d*, Dim stripe; c, clear stripe; *d'*, Dobie's stripe; *f*, a fibril of the same muscle. At the upper part the fibre has split transversely between the clear and dim stripes, and longitudinally between the sarcous elements. × 800.

At first the fibre shows no longitudinal striation. In a short time, however, a change takes place in the excised yet living muscle, whereby a regular system of thin, dark, longitudinal lines makes its appearance. They are most evident in the dim stripe (Fig. 97)—its substance being more refractile and less transparent than that of the clear stripe—but they are certainly continued through the clear stripe (Fig. 100). The longitudinal striæ are at regular intervals, and are the outlines of fibrils, of which the sarcous substance appears essentially to consist. Each fibril consists of segments of the dim, of the clear, and of Dobie's stripes (Fig. 97, *f*), and it is by the lateral apposition of the corresponding segments of neighbouring fibrils that the stripes of the fibre are composed. The segments which compose the dim stripe are the *sarcous elements* of Bowman, and these—as we shall see—constitute the contractile part of the fibre. The spontaneous revelation of the fibrillar outlines in the excised yet living and contractile fibre, is a phenomenon as difficult to explain as the spontaneous revelation of the nucleus in a newt's blood-corpuscle shortly after its withdrawal from the circulation (p. 57). The fibrils are enveloped and united by a small amount of interstitial substance, and it has been alleged that their revelation is due to an increase of this by the separation of fluid from the fibrils. In the frog and many other vertebrates the outlines of the fibrils do not become revealed so readily as in the dytiscus, but by prolonged maceration in dilute solution of chromic acid ($\frac{1}{4}$ per cent), or in weak alcohol, the interfibrillar substance is softened while the fibrils are hardened, so that, when the fibres are torn with needles, or subjected to pressure, they readily split into fibrils (Fig. 98). On the other hand, digestion for a short time in gastric juice, or maceration for some days in dilute hydrochloric acid (2 per cent), renders the sarcous matter prone to cleave transversely into a series of discs (Fig. 99). The transverse cleavage takes place between the dim and the clear stripes (Fig. 97). In the opinion of Bowman (*Op.* 53A, i. 152), "it is as proper to say that the fibre is a pile of discs, as that it is a bundle of fibrils; but, in fact, it is neither the one or the other, but a mass in whose structure there is an intimation of the existence of both, and a tendency to cleave in two directions." With Kölliker (*Op.* 45, p. 143), we dissent from this opinion, because cleavage into discs only takes place in macerated muscle, and even then it is rare; while the fibrils make their appearance in the yet fresh and living muscles—of the dytiscus and allied animals at all events. The dim and clear stripes are often spoken of as the dim and clear discs, but although such nomenclature is convenient when speaking of the fibre, it must be borne in mind that the *discs of the fibre* are mere optical expressions of certain regular arrangements of the dim and clear *prismatic segments of the fibrils.* In striped as in unstriped muscle, the essential morphological elements appear to be contractile fibrils.

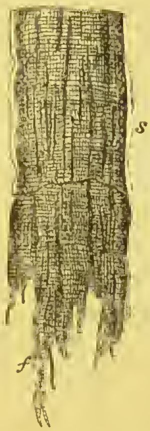

Fig. 98. Striped muscular fibre of frog, partially split into fibrils (*f*) after maceration in dilute chromic acid and dissection with needles. *s*, Sarcolemma torn across. × 300.

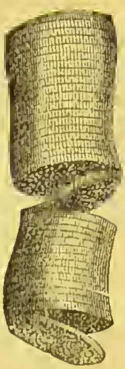

Fig. 99. Fibre o striped muscle partially split into discs. (Bowman.)

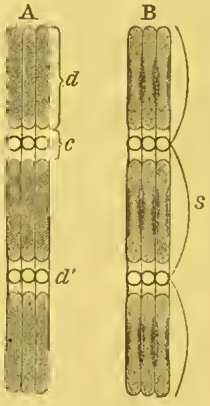

Fig. 100. A, Portion of a fresh striped muscular fibre of dytiscus after the revelation of the fibrillar outlines. *d*, Dim stripe; *c*, clear stripe; *d'*, Dobie's stripe. B, The same after forty-eight hours in $\frac{1}{2}$ per cent solution of osmic acid. *s*, Sarcolemma attached to Dobie's stripe, and swollen up by imbibition in the intervals. × 1200.

In the uncontracted muscle of the dytiscus, the dim stripe is three or four times the breadth of the clear stripe. Its aspect is homogeneous until the outlines of the dim fibrillar segments—the *sarcous elements*—become revealed. It is more refractile than the substance of the clear stripe, and has a somewhat pearly shimmer. The sarcous elements are prisms slightly rounded at the ends, and have—in their fresh state at all events—an apparently uniform calibre (Fig. 100, A), but in muscle which has been forty-eight hours or so in $\frac{1}{2}$ per cent solution of osmic acid they appear thinner in the middle than at the extremities of their shafts (B). Their transverse sections are somewhat angular (Fig. 101, *b*).

The sarcolemma is attached to Dobie's stripe (Fig. 100, B). The attachment, however, is not very intimate, for it may be ruptured by the imbibition of water. According to Krause (*Op.* 72, i. 83) Dobie's stripe is due to a thin membrane ("Krause's membrane") which traverses the whole thickness of the fibre, and is attached to the sarcolemma at its periphery. After much searching for this *membrane* we have failed to find it, but we have succeeded in seeing clearly a *single* row of highly refracting globules which appear to be the cause of Dobie's stripe (Fig. 100, A, *d'*). These globules were first indicated by Wagener (*Op.* 24, i. p. 118). *There is one globule in the course of each fibril.* It is difficult to say whether the globule is imbedded in the clear segment of the fibril, or forms a distinct partition in the middle of it. *When thrown slightly out of focus* a bright line crosses the centres of the globules, and there is then the appearance of a "double row of dots," in which manner they have been figured by several observers, and by myself (Fig. 96) before I had a lens capable of resolving the structure. These globules resemble a row of fine beads when the surface of the fibre is focussed and very carefully illuminated. Each globule has a light centre with a dark outline. In the fibre, and also in the isolated fibril, there is a slight bulging of the clear stripe opposite the globules of Dobie's line. The dip of the clear stripe on either side of them becomes more marked when the fibre or fibril is stretched. I have not been able to see any evidence of a lateral attachment between the fibrils in the position of Dobie's stripe such as exists between it and the sarcolemma.

The portion of the clear stripe on either side of Dobie's line consists of a feebly refractile soft substance. By some it is regarded as a fluid, but one might just as well, and with equal impropriety, regard protoplasm as a fluid. It has normally a homogeneous appearance, but often it is somewhat granular. The granules are fatty, and mostly lie between the fibrils. Unlike the substance of the sarcous elements, that of the clear stripe does not appear to be contractile. Both of them, however, are soft, extensible, and elastic. The general substance of the clear stripe is stained much less deeply by logwood and picrocarmine than the sarcous elements and the globules of Dobie's line.

For convenience I have spoken of the whole of the space between the ends of the sarcous elements as *the clear stripe*, regarding it as divided into two parts by the globules of Dobie's line. By those who believe in Krause's membrane, however, the clear stripe is described as intervening between it and the sarcous elements.

The appearance known as Hensen's stripe may be readily seen crossing the middle of the sarcous elements after they have been stained with logwood, each sarcous element being somewhat lighter in its centre than at its extremities. It may also be very clearly seen after the fibres have been macerated in ½ per cent osmic acid for forty-eight hours. Hensen's stripe is an optical effect for which it is difficult to account, but we are unable to find sufficient evidence of its being due to a less refractile segment in the middle of each sarcous element, as maintained by Hensen (*Op.* 23, 1868, p. 853).

The striped muscle of vertebrates differs, but only in details, from that of the dytiscus. The fibres and fibrils of the latter are broader, and their sarcous elements longer. In the uncontracted frog's muscle the dim stripe is rather less than twice the breadth of the clear stripe.

In a transverse section of striped muscle, frozen while living, and placed in contact with no fluid save blood-serum, the contents of the sarcous elements appear as dim, somewhat angular, areas, bounded by *clear* outlines (Fig. 101, *b*). According to Krause (*Op.* 72, p. 87) this appearance results from the separation of fluid from the sarcous elements, for when perfectly unchanged their transverse sections are bounded by thin *dark* lines, and their appearance therefore corresponds to the longitudinal view in Fig. 100, A. The fibrils are grouped into bundles, between which there is a ramifying system of lymph spaces. In the frog's muscle, but not in that of the rabbit or man, a nucleus occurs here and there between the fibrillar bundles (Fig. 101, *n′*), and in a similar situation there are highly refractile particles whose nature and significance are as yet doubtful (*a*).

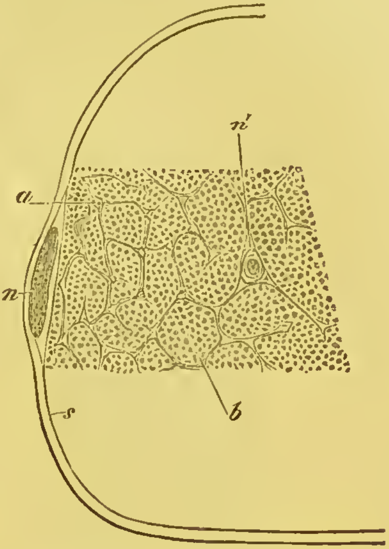

Fig. 101. Part of a transverse section of striped muscle of frog frozen while living. *s*, Sarcolemma; *n*, nucleus; *b*, ends of fibrils; *n′*, nucleus between the bundles of fibrils; *a*, clear particles in lymph spaces between the fasciculi of fibrils. × 1200.

Cohnheim (*Op.* 19, xxxiv. 606) was the first to describe the appearance of a transverse section of frozen striped muscle, but his drawings do not indicate the fascicular arrangement of the fibrils. The dim parts of such a section—which we believe to be the transverse sections of the sarcous elements—are often spoken of as "Cohnheim's areas."

It will be evident from the preceding that the view we hold regarding the structure of the striped muscle of the dytiscus, and which seems applicable to that of vertebrates, is that the sarcous substance in each fibre consists of bundles of fibrils with intervening lymph spaces, that the fibrils are surrounded by a small amount of clear interstitial matter, and that each fibril consists of alternate dim segments — the sarcous elements and clear segments — the latter containing in their middle part a bright refracting globule. The sarcolemma is attached to Dobie's stripe, but there is no sufficient evidence of a *membrane* crossing the fibre in the position of that stripe. Other views have, however, been advanced regarding this difficult subject, and it is proper that some of them should be stated.

It has been already indicated that, in the opinion of Krause, the fibre of striped muscle is divided transversely into a number of compartments by a series of membranes, which severally occupy the position of Dobie's lines, and are attached to the sarcolemma at their periphery. Merkel (*Op.* 65, p. 83), indeed, regards each transverse membrane of Krause as being in reality double. Krause further believes that a series of thin membranes are attached vertically to the transverse partitions dividing the sarcous matter into minute compartments or "caskets" (*Muskelkästchen*), each containing a "muscle element" consisting of a sarcous element, and at both ends of it a clear fluid representing one-half of a segment of the clear disc. He compares his "caskets" to the cells of a honeycomb. He regards the fibrils as entirely artificial, and consisting of a linear series of "caskets." Wagener (*Op.* 24, i. 118)—although he denies the existence of Krause's transverse membranes—believes in the vertical membranes, and supposes that the fibrils are severally enveloped by them. But, like Engelmann (*Op.* 24, ii. 124), we are not convinced of their existence. I feel obliged to entirely dissent from the opinion expressed regarding the structure of the striped muscle of the dytiscus held by Mr. Schäfer, and detailed by him in *Op.* 57. I have taken the muscle of the dytiscus as typical, because the structure of its fibrils appears to be essentially similar to that of vertebrate muscle. But it ought to be mentioned that in some other invertebrates the fully-formed striped muscle somewhat differs from that of the dytiscus. Thus Engelmann (*Op.* 17, xviii. 1) describes in the fibres of *Telephorus melanurus* a transverse row of rounded particles on both sides of the globules of Dobie's line.

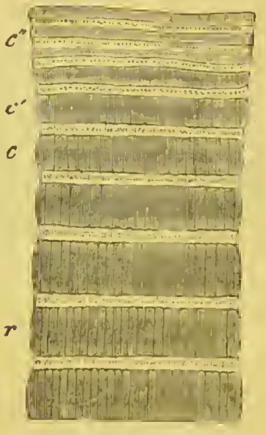

Fig. 102. Striped muscular fibre of dytiscus, relaxed at *r*, partially contracted at c and *c'*, completely contracted at *c''*. × 800. The figure shows the relative shortening of the dim and clear stripes in the contracted part. To avoid confusion the clear stripe has been kept light in the contracted part, although it really becomes darker than the dim stripe when viewed with direct light (see Fig. 103).

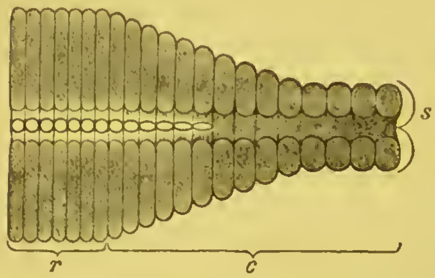

Fig. 103. Part of a striped fibre of dytiscus, showing one side contracted (*c*), and the other relaxed (*r*). *s*, Sarcolemma. × 1600. Drawn after fixation by osmic acid. The last three particles visible in Dobie's line to the right are represented as too oval, and the fully contracted sarcous elements are a little too narrow, and their dark outlines not quite broad enough.

APPEARANCE OF THE CONTRACTED FIBRE.—The striped muscle of the dytiscus is suitable for the study of contraction, because of the large size of its sarcous elements. If some fibres of the living muscle be dissociated with needles in sodium salicylate solution (one per cent) and examined immediately, one may see contractions of the fibres induced by the mechanical irritation, but they are too rapid and evanescent to allow of their successful study. After a few minutes, however, the fibres begin slowly to pass into the condition of rigor mortis. In dissociated fibres, its supervention is indicated by a slow and permanent contraction, that mostly begins at the cut ends of the fibres,—sometimes, however, at their sides. If a solution of osmic acid (one per cent) be added before the whole fibre is shortened, the contraction is arrested and the sarcous matter is killed and fixed in the several states of relaxation, of partial and of complete contraction. During contraction the fibre shortens and thickens, and it is not difficult to see that the *dim disc* is that in which the shortening principally occurs. In a fibre that has been severed from its detachments, and which is therefore free to contract to its fullest extent, the sarcous elements can be distinctly seen—especially after slight staining with eosin subsequent to the osmic acid—shortened to about one-third or even less of their original length (Fig. 103, *c*). In the *early stage* of contraction there is no perceptible change in the breadth of the clear stripe, but when the detached fibre is *fully contracted*, the clear stripe is only about two-thirds of its former breadth. This slight change in all likelihood results from its extension laterally by the thickening of the contracted sarcous elements. The sarcous elements therefore appear to be the contractile parts of the striped fibre, and the subdivision of the contractile substance into minute masses is a point of interest.

During contraction the clear stripe grows dim, indeed dimmer than the sarcous element stripe, and it becomes impossible—probably owing to the dimness—to recognise the particles of Dobie's line. This singular change may be well studied when there is a unilateral contraction of the fibre (Fig. 103). The first indication of the change is a thickening of the shadow at the ends of the sarcous elements, which during their contraction appear to become more refractile. The shadow deepens as they become more fully contracted, and eventually the shadows of the ends of the opposite sarcous elements appear to cross the clear stripe, and shade it completely, so that it becomes impossible to see the particles of Dobie's line (Fig. 103). Probably the thickening of the fibre is also a cause of the darkening during contraction, for in the contracted state *the sarcous element stripe also becomes slightly dimmer.* It is however possible, by a careful adjustment of the illumination, to render the clear stripe of the contracted fibre again lighter than the sarcous element stripe, which can always be recognised by its opalescent shimmer. At the margin of the contracted fibre the sarcolemma may sometimes be seen bulging slightly opposite the dim stripe, and dipping down to its attachment to the clear stripe (Fig. 103, *s*), but often there is no bulging.

APPEARANCE OF THE FIBRES IN POLARISED LIGHT.—When the fibres of striped muscle are placed under the micro-polariscope and examined in a field darkened by crossing the planes of polarisation of both Nicol's prisms at right angles to each other, those fibres which cut the planes of both prisms at angles varying from 0° to 90°, but especially at 45°, show a gray band in the position of each dim stripe, and a dark band in that of the clear stripe. Brücke (*Op.* 38, i. 235), who was the first to carefully investigate this subject, found that the sarcous elements are doubly refractile (*anisotropic*, ἄν - ισος unequal, τροπη bending), while the substance of the clear stripe is singly refractile (*isotropic*). The elements of Dobie's stripe also appear to be doubly refractile (Krause, *Op.* 72). Brücke found that the sarcous elements are uniaxial—the axis being longitudinal—and that their double refraction is positive like that of quartz. Since they remain anisotropic during contraction notwithstanding their change of shape, Brücke concluded that they contain minute mobile, doubly refractile particles (*disdiaclasts*, διακλάω to break), to which the anisotropic property of the sarcous element is referable. Martyn (*Op.* 73, iii. 233) has pointed out that a single fibril has no apparent influence on the polarised ray. Several sarcous elements must be superimposed ere any perceptible effect is produced.

The effect on the polarised ray may be most delicately shown by using, in addition to two Nicol's prisms, a mica or selenite plate below the object. When a fibre is placed at an angle of 45° to the polarising prism, and the analyser is slowly turned, the anisotropic parts pass through a succession of colours differing from that of the general field, while the isotropic parts—having no effect on the direction of the polarised ray—remain of the same colour as the field. Rouget (*Op.* 70, v. 247), on grounds that are altogether insufficient, maintains that the whole fibre doubly refracts light.

When the fibres of non-striped muscle are examined as above stated, they are found to be doubly refractile. Probably this property is possessed by the sarcous fibrils only.

COLOUR OF THE FIBRES.—The red colour of striped muscle is due to hæmoglobin which exists in the sarcous matter apart from that in the blood, as may be proved by muscle retaining its colour when all the blood is washed out of its capillaries. According to Ray Lankester (*Op.* 1, vi. 241), hæmoglobin is found in the pharyngeal muscles of some Gasteropods which have no hæmoglobin in their blood. As in the case of the blood-corpuscles, the fibres are red when seen in mass, but pale yellow when viewed individually.

W. Krause (*Op.* 71, p. 24) first pointed out that in the rabbit some muscles are red, of firm consistence and high elasticity, while others are pale, soft, and flabby. Amongst those that are red are the muscles of mastication, most muscles of the fore-limb, and several of those of the hind-limb, *e.g.* the semitendinosus and soleus. The adductor magnus, and most other voluntary muscles, are pale. Ranvier (*Op.* 11, 1874, p. 1) also finds that in the guinea-pig, skate, and torpedo there are similar differences. He observed that in the red muscles of the rabbit there are fusiform dilatations on the capillaries; but he showed that the redness of the muscle is assignable to the fibres themselves, and not to a greater amount of blood in the muscle, for when he washed the blood from the vessels of the red and pale muscles, the difference of tint remained. On comparing the fibres of the red semitendinosus with those of the pale vastus internus of the rabbit, Ranvier found that in the former the nuclei are more numerous, the transverse striation less, and the longitudinal striation more marked than in the latter. E. Meyer (*Op.* 24, iv. Ab. i. 110), however, has shown that the semitendinosus is exceptional, and that there is no notable structural difference between the other red and pale muscles of the rabbit. Ranvier (*Op. cit.*) discovered that both in the rabbit and skate the contraction of the red differs from that of the pale muscles in following the stimulus less rapidly and in lasting a longer time. This point has also been investigated by Kronecker and Stirling, and will be again alluded to in another place. Meyer (*Op. cit.*) holds that the tint of a muscle is conditioned by its function,—the more the muscle works the deeper does its colour become. This point, however, requires farther research. (Consult also W. Krause, *Op.* 72, p. 90).

RELATIONS OF THE FIBRES.—*a. To each other.*—The fibres of striped muscle are gathered into fasciculi of various sizes. Each fasciculus is enveloped in a sheath of ordinary fibrous tissue—the *perimysium externum* —which sends delicate processes between the fibres—the *perimysium internum* or *endomysium.* The processes of the internal perimysium do not form a continuous covering to the individual fibres (Fig. 104, *p*). In muscles that are more than an inch and a half in length a single fibre does not extend throughout the whole length of a fasciculus, and thus reach from one end of the muscle to the other, but the fibres terminate within the fasciculi in tapering ends (Rollett). At the end of the fibre the sarcolemma is intimately united with the perimysium, and through this with the ends of the neighbouring fibres. In addition to uniting the fibres throughout the length of a muscle, and thus enabling the contraction of each fibre in a muscle, however long, to be effective in approximating the ends of the muscle, the perimysium protects the fibres and also the blood-vessels and nerves from injury by external pressure.

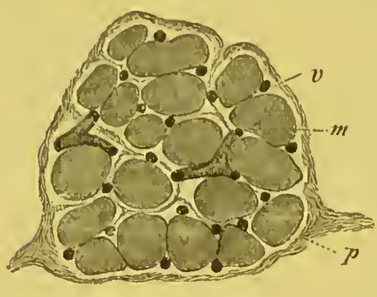

Fig. 104. Transverse section of a fasciculus of striped muscle with its capillaries (*v*) injected. *m*, Muscular fibres; *p*, perimysium. X 200.

b. To Tendon.—The attachment of the fibres of tendon to those of muscle is so intimate that it is impossible to separate them by mechanical means, and they sometimes have the superficial appearance of being continuous with the fibrillæ of the sarcous matter. But, according to Weismann, Fredericq (*Op.* 24, iv. 109), Ranvier (*Op.* 39, p. 503), and others, the sarcolemma always intervenes between the sarcous matter and the tendinous fibres. Ranvier demonstrates this by plunging the living muscle (of a decapitated frog) into water at 55° C. The sarcous matter is coagulated and forcibly retracted from the ends of the fibres, leaving the sacrolemma visible within the tendinous fibres.

It has not, however, been satisfactorily shown that there is not a union between the sarcous fibrils and the sarcolemma at the ends of the fibre. The undoubted attachment of the sarcolemma to Dobie's lines can be ruptured by means less violent than the irritating effect of hot water (see p. 128). On *à priori* grounds one would expect to find such a union, in order that the mechanical energy of the sarcous fibrils may be transmitted in a *direct* line to the tendon, as well as *indirectly* through the attachment of the sarcolemma to Dobie's lines. Ranvier maintains that the sarcolemma does not become fibrous at the ends of the fibre, as asserted by Wagener (*Op.* 24, iii. 100); but that it is merely joined to the fibrous tissue, either by a cement, or simply by a molecular union between the two. Wagener and Ranvier agree that it is impossible to dissolve the union by caustic potash, as Weismann asserted.

c. To Blood-vessels.—As might be anticipated from the energetic nature of the tissue, blood-vessels are numerous both in striped and unstriped muscle, particularly so in the striped muscle of mammals and birds. The veins and arteries usually lie together in the perimysium (Fig. 105, *a b*). The vessels within a fasciculus are capillaries (*c*). Most of them run parallel with the muscular fibres, and are united one with another by

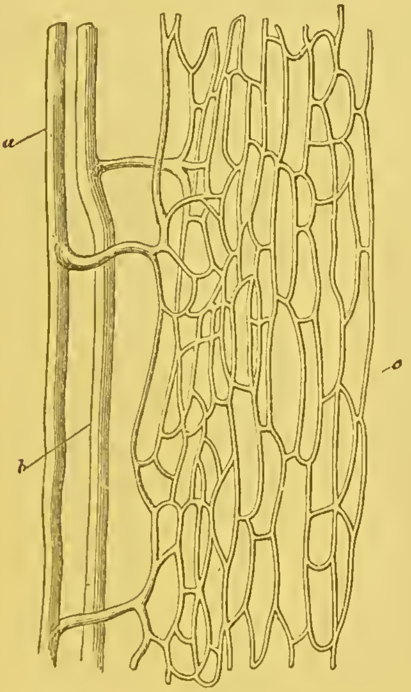

Fig. 105. Blood-vessels of muscle. *c*, Capillaries; *a*, small artery; *b*, small vein. × 250. (Kölliker.)

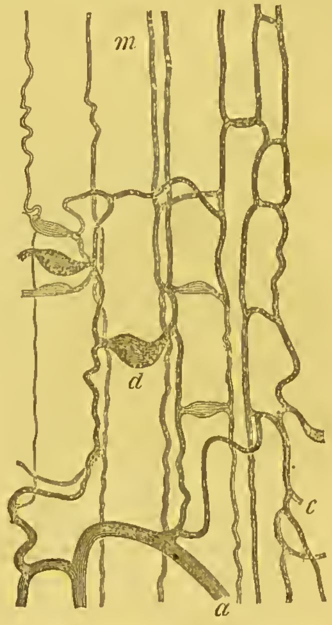

Fig. 106. Blood-vessels of a red muscle (*semitendinosus*) of a rabbit. *c*, Capillaries; *d*, dilatation on transverse branch of capillary; *a*, artery; *m*, position of a muscular fibre. (Ranvier.)

transverse branches. The capillaries all lie outside the sarcolemma (Fig. 104, *v*), so that the nutrition of the sarcous matter has to be carried on by diffusion through that membrane.

In the red, as distinguished from the pale, muscles of the rabbit, Ranvier has observed fusiform swellings on many of the transverse branches of the capillary network (Fig. 106, *d*). He points out that these dilatations must constitute minute reservoirs for blood, which are probably of service in giving an increased supply of oxygen and pabulum to these hard-working muscles (see p. 132).

d. To Lymphatics.—The lymphatics of muscle have been as yet but little investigated. Schweigger-Seidel (*Op.* 38, i. 255) found that the network of lymphatics under the pericardium is continuous with numerous lymph spaces between the muscular fibres—in the general substance of the heart. By the silver process he found that the intermuscular lymph spaces are lined by a layer of endothelium. Probably in muscle generally, all the spaces in the endomysium around the muscular fibres and capillaries are lymph spaces in which the lymphatics take origin, but although Loewe (*Op.* 72, p. 93) states that the sarcolemma is covered by the endothelium of surrounding lymph spaces, the subject has not as yet been sufficiently investigated.

e. To Nerves.—The termination of nerves in striped and in unstriped muscle will be described with the nervous system.

The Muscular Fibres of the Heart.

The cardiac muscular fibres are striped, but they have certain peculiarities, both structural and functional, which place them in a position intermediate between the unstriped and the ordinary striped muscle. There is no sarcolemma, and each fibre has one, rarely two, nuclei placed in its central part. Throughout the general substance of the heart, the muscle cells are short cylinders which anastomose with neighbouring cells, either by short branches or by their longitudinal surfaces;

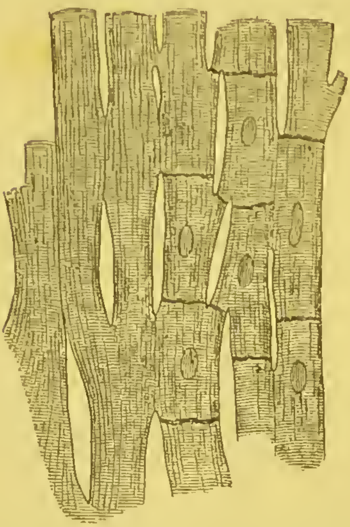

Fig. 107. Network of muscular fibres from the general substance of the mammalian heart. On the right, the limits of the separate cells are somewhat diagrammatically represented. (Schweigger-Seidel.)

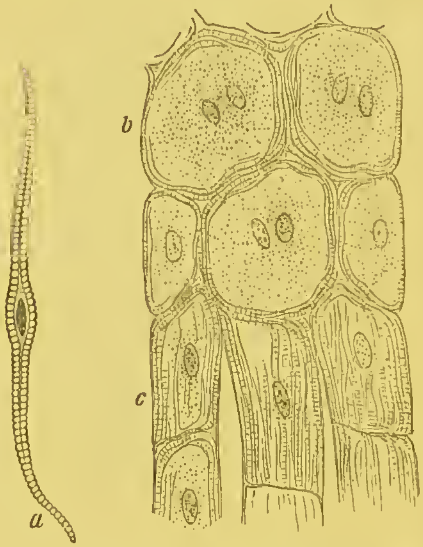

Fig. 108. *a*, Fibre from general substance of frog's heart (Ranvier). *b*, Purkinje's fibres from beneath the endocardium of a sheep; *c*, transition between Purkinje's fibres and the general fibres. X 300.

they thus form retiform lamellæ with narrow interspaces. The somewhat sinuous ends of the cellular segments abut one upon another, and are united by a clear cementing substance which may be blackened by silver nitrate, and dissolved by caustic potash. After treatment with potash the cellular segments of the reticulum may be readily dissociated (Eberth).

In the frog's heart tho networks are composed of spindle-shaped fibres not unlike those of unstriped muscle, but differing from them in being transversely striped (Weismann).

Purkinje's Muscular Fibres.—Immediately under the ventricular endocardium of ruminants there is a gray gelatinous-looking network, first described by Purkinje. It consists of bands of polyhedral cells, each having a cortex of striated sarcous substance enclosing a core of undifferentiated protoplasm with one or two nuclei. There are transitional forms between these cells and the general cardiac fibres (*c*), of which Purkinje's cells appear to be an arrested development. (Consult Schweigger-Seidel, *Op.* 38, i. 244; and Ranvier, *Op.* 39, 535.)

The *functional* characters of the cardiac muscle also place it intermediate between unstriped and ordinary striped muscle, inasmuch as its contraction takes place more slowly, and is more prolonged than that of ordinary striped muscle.

Development, Growth, and Atrophy of Muscle.

Development and Growth.—The fibres of unstriped and of striped muscle are developed from the cells of the mesoblast. Each cell is at first a nucleated particle of protoplasm without an envelope. The cells are at first rounded, and become elongated into fibres as development proceeds.

When a cell becomes a *non-striped fibre* the nucleus usually remains single in the centre of the fibre. The protoplasm becomes modified into contractile fibrils, while the periplast (the sarcolemma) makes its appearance around it. There is nothing to lead one to suppose that the sarcolemma results from the transformation of a special set of cells. Probably it is simply produced from the protoplast which it encloses, but the precise mode of its formation has yet to be made out. Non-striped muscle may also be developed from cells resembling connective tissue corpuscles; as may be seen in the bladder of the salamander (Flemming, *Op.* 18, xiii.) In the uterus during pregnancy new muscular fibres are developed from small round granular cells (Kölliker). The origin of the latter has yet to be made out.

Each fibre of *striped muscle* is in the embryo developed from a *single* mesoblastic cell (Remak). In producing a *cardiac fibre* the embryonic cell enlarges, its protoplasm becomes transformed from without inwards into striated sarcous matter, and the nucleus, either single or divided into two, remains in the centre of the cell, enveloped in a small quantity of undifferentiated protoplasm. The cells become elongated, branched, and joined together. As already stated, Purkinje's cells are to be regarded as the result of arrested development.

In producing a fibre of *ordinary striped muscle* the mesoblastic cell enlarges and becomes fusiform, the nucleus repeatedly divides, and the protoplasm is gradually transformed into striated sarcous substance from the periphery inwards. When this has proceeded to some extent a fibre of *mammalian* striped muscle is a tube of fibrils enclosing a core of undifferentiated protoplasm with many nuclei. But as development proceeds, the nuclei, with some protoplasm, leave the centre and appear at the periphery of the fibre. Probably they move outwards in the spaces between the fibrillar bundles. But in the striped muscle of the *frog* the nuclei are at an early period of development all placed outside the striated substance. Many of them continue there as the nuclei under the sarcolemma, whilst some of them appear to move into the interior of the fibre and remain permanent between the fibrillar bundles (Ranvier, *Op.* 39, 515).

With regard to the origin of the sarcolemma of striped muscle, all are agreed that it does not exist at an early stage in the development of the fibres, but its mode of formation is disputed. Kölliker regards it as nothing but a cell-membrane produced around the protoplasm. This idea is supported by the observations of Wilson Fox (*Op.* 3, year 1866), and by Calberla (*Op.* 24, iv. 111). Wolff (*Op.* 24, vi. 101), however, regards it as a transformation of special cells which disappear in the process. It must not, however, be forgotten that the muscle-corpuscles may be readily mistaken for such cells, and that in the case of non-striped muscle—where there are no peripherally placed muscle-corpuscles, there is no evidence of the production of the sarcolemma from special cells. Probably in both cases the sarcolemma is merely a cell-membrane.

The fibres of striped muscle are also developed after embryonic life has ended. Much of the enlargement of growing muscles is due to an increase in the number of the fibres, but the origin of the new fibres still requires elucidation.

Their development is to be seen in the frog during the spring time, when those striped fibres which have wasted during the winter are replaced by new ones. Two modes of development are described—1. Weismann and Kölliker state that new fibres result from a longitudinal cleavage of the old ones. 2. According to Von Wittich they spring from connective tissue corpuscles. In the testis and ovary, where tumours of striped muscle sometimes, though rarely, arise, connective tissue corpuscles, or at all events blood-leucocytes, appear to be their source.

It is commonly stated that when striped muscle is destroyed it is not regenerated in warm-blooded animals, and that when cut across or partly removed the breach is healed, not by new muscle, but by fibrous tissue. In a recent research, Kraske (*Op.* 24, vii. Ab. i. 75), working under the direction of Cohnheim, has shown that when the striped muscle of the rabbit is cauterised by the interstitial injection of carbolic acid, no fibrous cicatrix appears at the cauterised spot, but in the course of six weeks it is filled up with newly developed muscle. He finds that the sarcous substance of the old fibres disappears, the muscle-corpuscles proliferate and grow spindle-shaped. The sarcolemma vanishes, and the liberated muscle-corpuscles severally become striped fibres.

In a growing muscle there is not only an increase in the number of the fibres, but the *individual fibres grow larger;* thus, the striped fibres of the adult are longer and about five times broader than those of the newly-born child. According to Frey, the enlargement is due to interstitial growth. This theory seems to hold in the case of the growing non-striped fibres of the pregnant uterus, and probably it also to some extent holds as to those of striped muscle, but there is certainly another way in which the latter grow. The nuclei under the sarcolemma multiply, the protoplasm around them increases in quantity, and is converted into sarcous matter. This mode of growth may be seen in many of the fibres of the diaphragm of young and also of adult mammals (Klein, *Op.* 69, p. 80). A similar change takes place in striped muscle elsewhere, when it is subjected to *prolonged and systematic exercise.*

Although it is true that exercise favours the growth of muscle—and no bodily organs are so much affected by exercise as the muscles—it is equally true that they grow without exercise; thus, in the fœtus, the muscles of respiration, those of the tongue, jaws, and other parts that are *not exercised*, grow and are ready for work at birth. Their growth seems only referable to the trophic and germinal energy of the tissue, *possibly* aided by a trophic influence of the nerves. The growth of the muscular fibres of the pregnant uterus is probably in large measure due to the increased supply of pabulum resulting from the marked dilatation of the blood-vessels. This, however, is insufficient to explain the development of new fibres, and therefore it may be assumed that there is a trophic and germinal excitement in the tissue elements of the uterine wall, to which the vascular dilatation is only an adjuvant. Of the influence of exercise upon the muscular growth, the marked development of the muscles of the blacksmith's arm, and the thickening of the wall of the heart when in abnormal states of the circulation it is compelled to exert itself more forcibly, are well-known illustrations. The explanation is probably this: 1. The functional excitement of a muscle not only induces a discharge of mechanical energy, but seems to excite the trophic and also the germinal energy of the tissue, and thus leads to an increase of its nutrition, and it may be to the production of new tissue. 2. When a muscle is thrown into contraction, its blood-vessels at the same time undergo a dilatation, whereby an increased supply of pabulum is brought to the seat of labour, and the growth of the tissue thus favoured. The muscular growth induced by exercise is not, however, capable of indefinite extension; a maximum is attained which varies in different cases.

ATROPHY.—When muscles whose growth has been favoured by exercise are too little used, or allowed to remain completely at rest, they undergo a partial atrophy, for reasons which may be inferred from the foregoing. A familiar illustration of the fact is to be found in the emaciated limbs and flabby muscles of one who has for a long time been confined to the recumbent posture. In such cases, however, it is to be observed that the muscles nearly always retain their contractility, if their nerves be not paralysed, and if the circulation in them be maintained.

The atrophy of muscle is, however, most marked in cases of nervous paralysis; thus, when the nerves of a muscle are divided and their reunion prevented, simple atrophy, and atrophy through fatty degeneration supervenes, in the course of some months contractility is lost, and finally the muscle becomes a band of little more than connective tissue. The course of the degeneration in such a case may be retarded by systematically exercising the muscle by electrical stimulation (John Reid, *Op.* 80, p. 1), but unless the nervous paralysis disappear, the muscle eventually loses its contractility, although several months may elapse ere this ensue (*Op.* 76, i. 137). Nervous paralysis therefore produces an effect on the nutrition of muscle which is not explicable on the theory that it is entirely due to defective exercise. By some it is supposed that the nerves have a direct *trophic* influence on the nutrient processes in the *passive as well as in the active* muscle, but this question will be considered in another chapter.

Atrophy through fatty degeneration is apt to supervene in the inactive muscle, and always does supervene in muscle whose nerves are permanently paralysed. The fat gradually appears in the sarcous matter, and by taking the place of it, the fibre is rendered useless. It is probable that in *consequence of diminished trophic energy* the molecular structure of the tissue tumbles to pieces, and that the molecules of myosin—the chief proteid of the muscle—disintegrate, and in so doing yield molecules of fat. But fatty degeneration sometimes occurs in a muscle which is not inactive. Thus, in the heart, it is not an uncommon change in advanced age. Probably it is here also the result of a diminution in the trophic activity of the tissue. Its occurrence in the muscular fibres of the uterus after parturition, and its leading to the disappearance of most of them, is a physiological event assignable to the same cause. But the inactivity of muscle is not *necessarily* followed by fatty disintegration; it does not appear in the uterine fibres previous to parturition, although they are inactive, nor does it appear in the respiratory muscles of the fœtus, although they are for some months inactive. The probable explanation of this apparent anomaly is, that the trophic energy of the growing fibres of the uterus and of the child seems to be so great that exercise is not required to prevent atrophy. The question of the atrophy of muscle, however, chiefly belongs to pathology, and works on that subject must therefore be consulted for further details.

As the *chemical composition* of muscle will be best understood after that of the blood has been studied, and as the chemical changes occurring in the tissue involve questions relating to the food and excrementitious matters of the body, they will be discussed in a future chapter.

The Elasticity of Muscle.

Seeing that muscles are organs for the performance of mechanical work, and since their manner of working consists in overcoming resistance by a forcible diminution of the length of their fibres, it is important to study their behaviour when subjected to a force of *linear* extension, and when they are liberated from the influence of such a force.

When stretched lengthwise, a muscle readily extends. When liberated from the stretching power, it regains its former length, provided it has not been overstretched. Its elasticity is therefore *small in amount*, but *perfect in quality*. The energy of restitution, or, in other words, the *elastic energy* of a body, cannot be greater than the energy used to displace its particles; therefore, since a small amount of energy is needed to extend a muscle, its elasticity is *small in amount*, although its molecular structure allows it to induce a recoil which under normal circumstances is *perfect*. There is, however, in the case of muscle, as in that of other elastic solids, a *limit of elasticity*,—that is, a degree of extension beyond which the muscle cannot be stretched without suffering a permanent change of form. Beyond this limit the elasticity becomes *imperfect*.

To some extent the elasticity of muscle resembles that of an india-rubber band. The latter being very extensible, its elasticity is small in amount, but within a certain limit its quality is nearly perfect. The two bodies, however, differ remarkably in the ratio between the extending force and the resulting extension. If a vulcanised india-rubber band be suspended, its length measured, and weights successively applied, it is found that *the extension is proportional to the weight*, that is, equal increments of weight are followed by equal increments of length; thus, if a weight of 10 grammes extend the band 4 millimeters, 20 grammes will extend it 8 millimeters, and so on. This law holds for other inorganic solids, but in those that are organic, with the exception of bone, the extension is *not proportional to the weight;* the first weight has a greater effect than the second, the second than the third, and so on.

Facts such as the above are most readily ascertained by the graphic method of recording movement. The most accurate method is the following: An elastic band is suspended by a rigid support. Its lower end is clamped to a rod bearing at right angles to it a writing style. The rod and style glide between parallel bars, so that only a vertical motion is allowed. The free end of the style is placed against a plate of smoked glass, or a cylinder covered with smoked paper. A pan for weights is hooked to the lower end of the style-bearing rod. The observation is begun by drawing the plate across the style to obtain an abscissa (Fig. 109, *o x*), indicating the position of the unstretched band. The plate is then shifted until the style is near one end of the abscissa, and a weight of say 10 grammes is applied (*a*). About 20 seconds are allowed for the completion of the resulting extension. The plate is then drawn a little to one side, an additional weight of 10 grammes applied (*b*), and so on. The result is a figure like a stair descending from the abscissal line. The steps are of equal depth, indicating equal increments of extension for successively equal weights. If the glass plate were carefully drawn to precisely the same extent after the application of each successive weight, the geometrical expression of the figure would be exact; but as the experimental detail of this is often difficult, it is easier to be indefinite in moving the plate, and then to construct a precise geometrical figure on a separate paper, by drawing an abscissal line, dividing it into equal sections, and projecting ordinates below each point of division to the same extent as that of the tracing. A line is drawn to touch the lower end of each ordinate and the point *o* of the abscissa. The line thus obtained (Fig. 109, *s*) is the line of elasticity, a straight line in the case of elastic inorganic solids (Wertheim), including india-rubber (Marey, *Op.* 74, p. 301). If now the same experiment be repeated with the gastrocnemius,

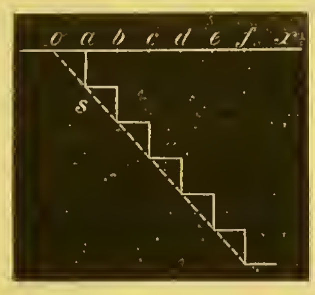

Fig. 109. s, Line of elasticity of an inorganic solid, such as india-rubber, indicating effects of equal increments of weight applied at *a*, *b*, *c*, *d*, *e*, *f*; *o x*, abscissa (see text). (Marey, slightly altered.)

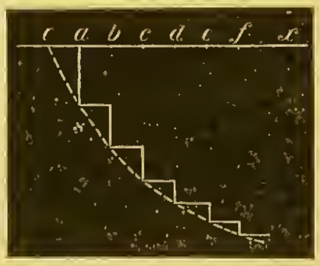

Fig. 110. -s. Line of elasticity of an organic solid, such as a muscle, indicating the effects of equal increments of weight applied at *a*, *b*, *c*, *d*, *e*, *f*; *o x*, abscissa (see text). (Marey, slightly altered.)

or, better still, because of its parallel fibres, with the sartorius muscle of a frog, the tracing obtained resembles Fig. 110. The increments of extension are not proportional to the increments of weight, but are in a diminishing series. The curve of elasticity (*s*) is very nearly a hyperbola.

Pflüger's myograph (Fig. 111) may also be used for such observations as the above. The band or muscle is fixed in a rigid support and joined to a lever (*l*), whose moving end bears a style for recording the movement on smoked glass (*g*). The lever, however, is in this case open to objection; for, by moving in an arc, it does not in any two positions move to precisely the same extent, although the elastic body to which it may be attached suffers equal increments of extension. The variation may, however, be discarded when the lever is horizontal, or nearly so.

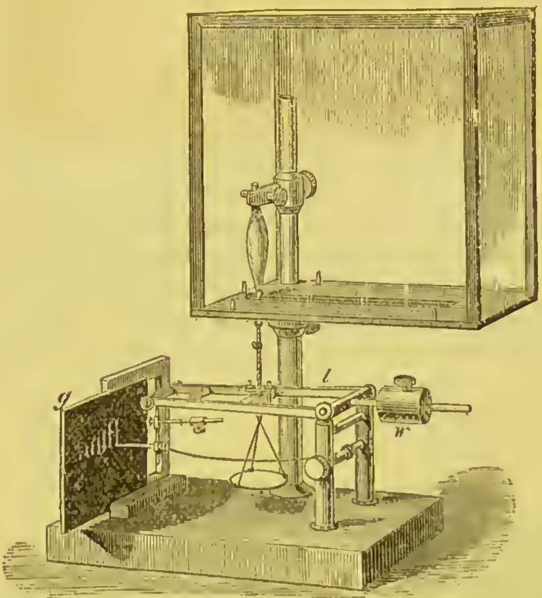

Fig. 111. Pflüger's myograph. *l*, Lever; *w*, counterpoise; *g*, smoked glass; the muscle is placed in a moist chamber.

Marey (*Op.* 74, p. 298) has directly obtained the curve of elasticity by attaching a lever to the gastrocnemius of a frog, and causing it to record its movement on a slowly-revolving cylinder, while the muscle is gradually stretched by a vessel into which mercury is allowed to flow. When the curve of extension (Fig. 112, *s*) indicated scarcely any further elongation the muscle was allowed to slowly recoil by letting the mercury gradually escape from the vessel. The curve of recoil (*r*) is, like that of extension, hyperboloid. The curves of extension and recoil together constitute the complete curve of elasticity. The abscissæ *o x* and *o′ x′* respectively indicate the position of the point of the lever before and after extension, and show that the elastic recoil of the muscle was imperfect; the limit of its elasticity having been passed. Marey (*Op. cit.* p. 301) finds that in frog's muscle the limit is easily passed, for, while the gastrocnemius can lift a weight of 1200 grammes without rupture, it does not completely recoil after having been stretched by a weight of 100 grammes.

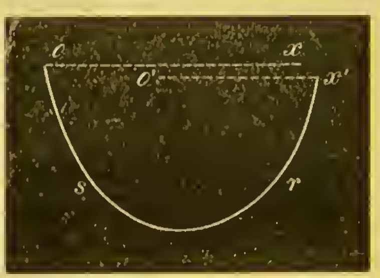

Fig. 112. Curve of elasticity produced by the gradual extension (*s*) and recoil (*r*) of a frog's muscle; *o x* and *o′ x′*, abscissæ before and after stretching. (Marey.)

Elastic After-action.—When a weight is applied to a muscle, there is a sudden, and then a more gradual elongation. When the weight is removed, there is a sudden, and then a more gradual recoil. Thus Fig. 113 is a tracing taken from a fresh gastrocnemius of a frog, with a lever similar to that of Pflüger's myograph applied to a slowly revolving cylinder. The abscissal line previous to stretching (*a*) has been prolonged as a dotted line to indicate its relation to the elastic curve. A weight of 100 grammes was applied to the muscle at *b*, and removed at *d* after the lapse of a minute. At *b* there is a sudden extension, followed by a slow after-extension (*c*). At *d* there is a sudden shortening, followed by a slow after-shortening (*e*), which does not, however, raise the abscissal line (*f*) to the level of the first abscissa (*a*), because the muscle had been over-stretched; *c* and *e* are the two phases of the *elastic after-action.*

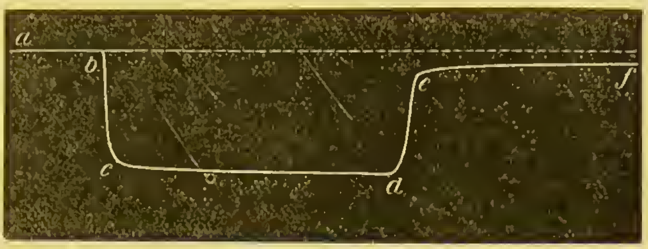

Fig. 113. Elastic after-action of frog's muscle (see text).

Muscular Tonicity.—Even in their relaxed condition the muscles are in a state of slight tension, termed their *tonicity*, in consequence of which they feel firm and not flabby. In virtue of this condition, a muscle retracts when it or its tendon is divided, and the wound gapes, although the muscle is in a state of relaxation. This muscular tone has been ascribed to a slight contraction of the muscle, but there is no evidence that it is due to anything more than its elasticity. Were it due to contraction it ought to disappear when the nerve of the muscle is divided; but section of the nerve is not immediately followed by the slightest elongation of the muscle (Heidenhain, *Op.* 49, 1856), although in course of time, apparently owing to impaired nutrition, the tonicity does disappear. The so-called tone of the sphincters of the anus and bladder is not an elastic effect, but a real contraction kept up by nervous impulses passing from the spinal cord.

Observations by Donders and Mansvelt (*Op.* 78) on the human biceps, and by Roy (*Op.* 2, i. 472) on the frog's heart, show that the elasticity of muscle is diminished by *fatigue.* Roy's experiments also prove that it is diminished by *defective nutrition.* Continued diminution of the elasticity of the cardiac fibres ends in their permanent extension, and the serious pathological condition of cardiac dilatation is the result. The elasticity of muscle is also diminished in *weak* and *relaxed conditions of the system.* A flabby state of the tongue is a sign of it. At *death* the elasticity increases *in amount*, but becomes *less perfect;* the muscles are therefore less extensible, and, when stretched, recoil less perfectly.

E. Weber (*Op.* 75) found that if the same weight be applied to a muscle during its states of relaxation and contraction, it produces a relatively greater extension in the contracted muscle; from which he inferred that during contraction elasticity is diminished. He further stated that, if a muscle be stretched by a weight so heavy that it cannot contract, a slight elongation occurs when the muscle is stimulated; from which he inferred that the altered elasticity is due to a molecular change induced by stimulation. Weber's method of experimenting was rough, and probably for that reason the latter observation has been found by Wundt (*Op.* 77, p. 574) to be incorrect. There is therefore no evidence of any change in the elasticity during the active condition of muscle. This conclusion is supported by Kronecker and by Donders. The greater extension produced by a weight in a contracted as compared with a relaxed muscle, appears to be owing to a diminished shortening of the muscle during contraction because of the resistance offered by the weight.

FUNCTIONS OF THE ELASTICITY.—The elasticity of muscle discharges important functions. In virtue of it, the muscles in their relaxed condition are in a state of slight tension, so that, at the instant of contraction, *time is not lost, nor is energy wasted, in bracing them up.* The smallness in the amount of the elasticity is of service in offering little resistance to the contraction of antagonistic muscles.

Muscular elasticity is also of great service in *lessening the shock of contraction*, for, as the tendons are inextensible, a sudden and powerful contraction would readily tend to rupture the muscle, and would produce a violent shock throughout the system if the muscles were not elastic. The elasticity diminishes the abruptness of the movement, and—as will afterwards be shown—it also fuses into a uniform steady pull the rapid succession of short contractions of which any ordinary voluntary movement consists. It also *lessens the dissipation of energy*, for, as shown by Marey (*Op.* 74, p. 457), "when a force of short duration is employed to move a mass, a more useful effect is obtained when it acts through an elastic medium." [1]

THE EXCITABILITY OF MUSCLE.

Living muscle possesses excitability (irritability), in virtue of which it may be thrown into a state of excitement, and the potential energy of its molecules liberated (p. 10). As the most important and obvious—although not the only—sign of excitement is contraction, the term contractility is sometimes for convenience substituted for excitability in speaking of a contractile tissue, but, strictly speaking, the term contractility means the working power of the muscle. That it is necessary to distinguish excitability from contractility is shown by the fact that *excitability* is increased while *contractility* is diminished by the presence in the muscle of an excess of the effete substances creatin and lactic acid (Ranke).

Muscle may be thrown into contraction by stimuli of a nervous, electrical, thermal, mechanical, and chemical nature.

1. NERVOUS STIMULATION.—In all the higher animals the stimulation of muscle normally springs from its nerve. As the intra-muscular nerve terminations will be described in the chapter on nerve tissue, it need only now be stated that the nerve fibrils come into very close relation with the sarcous substance, so that the nerve energy can readily affect it.

2. ELECTRICAL STIMULATION.—Of all the artificial stimuli of muscle and nerve, electricity is that most commonly had recourse to, because of the readiness with which it can be applied, the ease with which its intensity may be graduated, and its non-injurious effects on the tissue when carefully used. Both galvanic and faradic electricity are employed. The tissue to be stimulated is made a part of the electrical circuit, and the electrodes through which the stream passes between the wires of the electromotor and the tissue are in ordinary physiological experiments a

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[1] In harmony with these facts, Marey (*Op.* 79, p. 124) points out that if an elastic medium be interposed between a motor power and a load, *e.g.* between a horse and a vehicle, shocks are lessened and work economised.

pair of insulated wires or plates of copper or platinum. But when it is important to avoid the currents generated by the contact of moist tissues with copper and even with platinum, *non-polarisable* electrodes are required.

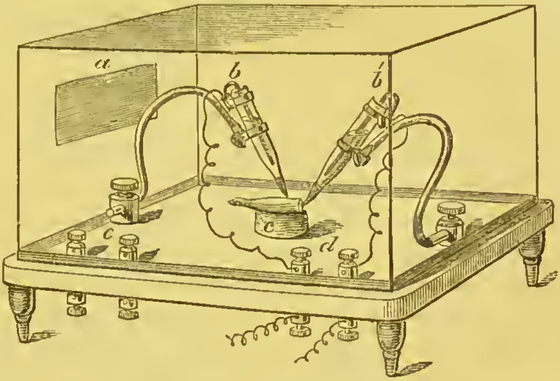

Fig. 114. Moist chamber used in various experiments on muscle and nerve. It consists of a vulcanite table with a glass shade. The air is kept moist by wet blotting paper (*a*); *b b′*, Non-polarisable electrodes fixed to flexible leaden rods; *c*, paraffin block with a muscle on it.

The non-polarisable electrodes of Donders are often used. They consist of a pair of glass tubes (Fig. 114, *b b′*) closed at their lower ends with plugs of sculptor's clay moistened with water or very dilute solution of sodium chloride. The contact of nerve or muscle with clay so prepared yields no electricity. The tubes are partially filled with a saturated solution of pure zinc sulphate, into which there dips a rod of pure amalgamated zinc, to which a wire of the circuit is attached. This arrangement is needed, because the contact of a copper wire with the moist clay generates a current. Unfortunately the solution diffuses through the clay, and renders it useless in the course of a day.

The non-polarisable electrodes of Fleischl are preferable to the above. They consist of a pair of small tubes closed at the lower ends with plaster of Paris, in the centre of which a small camel-hair brush is included. One half of the brush projects free from the plaster plug, and is the terminal to which the tissue is applied. It is moistened with saliva, or dilute sodium chloride solution (1 per cent). The other arrangements in the tubes are the same as in Donders' electrodes.

The electrical circuit is closed and opened by various forms of electrical keys. Those most convenient for experiments on stimulation of the tissues are (1) a key with a platinum contact, such as the Morse telegraph key; and (2) a mercurial key where the contact is made by dipping a copper, or better, a platinum wire into mercury. The mercurial key is to be preferred in all cases where successive shocks of uniform intensity are desirable. For this purpose the surface of the mercury must be kept perfectly clean, and the production of sparks prevented. This object is best attained by the mercurial key devised by Kronecker and Stirling (*Op.* 1, ix. 318), in which the surface of the mercury is continually washed by a stream of dilute alcohol.

a. Stimulation by Galvanic Electricity.—In physiological experiments the voltaic elements of Grove, Daniell, and Léclanché are commonly used. Grove's elements of small dimensions are the most convenient.

When a galvanic stream of sufficient intensity is sent along the nerve of a physiological limb (Fig. 1), the nerve is stimulated and the muscle thrown into contraction at the closure or opening, or at both the closure and the opening of the circuit. There is no stimulation of the nerve during the interval of flow, provided the intensity of the current be constant; but if the intensity be varied suddenly and sufficiently, the nerve is excited. Analogous results are obtained when the *sensory* fibres of a nerve-trunk are made the subject of experiment. It may therefore be formulated as a law that a galvanic stream stimulates a *nerve-trunk* only when it enters and when it leaves the nerve, but not during the period of its flow unless it undergo variations of intensity (Du Bois Reymond). It will be afterwards shown, however, that the vital properties of the nerve are affected during the entire period of flow.

But when the *peripheral terminations of sensory nerves—e.g.* those of the skin or tongue—are traversed by the stream, they are stimulated during the entire period of flow as well as at the moments of entrance and departure. The result is a constant pricking and burning sensation in the case of the skin, and a metallic taste, with a burning and pricking sensation, in that of the tongue. *Muscular fibres* are affected in the same sense as the peripheral sensory nerve terminations. Thus, on stimulating a *muscle directly* with a galvanic stream just strong enough to give a reaction, contraction occurs at the closure and opening of the circuit; but on increasing the strength of the current, a state of *constant contraction* (tetanus) ensues. The reaction of the muscle is therefore for the most part similar to that of peripheral sensory nerve terminations, and the question arises, Is the muscular reaction due to a direct effect on the muscular fibres, or on the terminations of the motor nerves, or on both? The question can be partially answered by *physiologically eliminating* the nerve terminations through the paralysing influence of curara. That this poison really does paralyse the nerve-ends must be assumed until the proof is furnished and explained (p. 151). The curarised muscle requires a somewhat stronger current, but the reactions given both by the weak and stronger currents are similar to those of the non-curarised muscle. Therefore the effect of a galvanic current on muscular fibres differs from its effect on nerve fibres, and resembles that on peripheral sensory nerve terminations. Whether or not the motor nerve terminations are affected in a manner similar to the sensory nerve terminations is as yet unknown.

In both nerve (Pflüger, *Op.* 81, p. 453) and muscle (Von Bezold, *Op.* 82, p. 266) stimulation occurs only at the – pole (*cathode*[1]) when the circuit is closed, and only at the + pole (*anode*) when it is opened. This may be readily shown by laying a curarised frog's sartorius upon a pair of non-polarisable electrodes, with a considerable length of fibres between them. In a curarised muscle the transmission of excitement is delayed because of the nervous paralysis, and it may be observed, especially when the muscle is fatigued, that, on *closing* the circuit, a contraction wave appears at the *cathode* and rapidly travels along the muscle, while at *opening* the wave begins at the *anode*. The use of a magnifying glass is of service in this experiment. If the muscle be partially cut across between the electrodes, the cut may be seen to gape towards the – pole at closing, and towards the + pole at opening the circuit (Engelmann, *Op.* 83, p. 340; Romanes, *Op.* 1, x. 730).

The effect of an electrical current on muscle is most powerful when it is sent *along* the fibres.

b. Stimulation by Faradic Electricity is the most common method of excitement in physiological experiments, because of the readiness with which currents of almost any desirable strength can be obtained by induction from the galvanic stream of a single voltaic cell. The faradic electromotor commonly used depends on the principle that if two electrical circuits be placed in proximity but not in contact, and a galvanic current sent through one of them, an *instantaneous* current is induced in the other at the moment when the galvanic stream enters and when it leaves its circuit. The inducing and induced currents are distinguished as *primary* and *secondary*. The secondary current, induced by *closing* the primary circuit, has a direction the *reverse* of that in the primary circuit, whilst that induced at *opening* has the *same* direction. There is therefore a *constant reversal* in the direction of the induced currents, whilst that of the inducing currents remains unchanged. Currents may also be induced in the secondary circuit by merely varying the intensity of the primary stream; an increase of intensity induces a current in the same direction as the closing of the primary circuit, and conversely. In the induction machine (Fig. 115) the wires of the primary and secondary circuits are coiled into two spirals (R and R′), in order that the effect of the primary circuit may be intensified. The primary wire is short and thick, to offer as little resistance as possible to the galvanic stream, the tension of which is low. The secondary wire is much thinner, in order that many coils may go into small space. The tension of the induced currents being high, and the electrical resistance of any of the tissues so much greater than that of the coil, a long wire in the secondary spiral has no disadvantage. The wires of both coils are insulated. A bundle of soft iron wire is placed inside the primary spiral. The current in the latter magnetises the iron, and as the introduction and withdrawal of a magnet from within a coiled wire occasions induced currents, the magnetisation and demagnetisation of the iron intensifies the effect of the primary upon the secondary spiral. The strength of the induced currents may, for physiological purposes, be conveniently varied by altering the distance between the spirals, as in Du Bois Reymond's electromotor (Fig. 115). The secondary spiral is made to slide upon a grooved board, so that it can be pushed around the primary spiral to obtain the strongest induction effect, and drawn from it to obtain currents of less intensity. The strength of the induced currents is inversely as the square of the distance between the spirals. A millimeter scale is attached to the board, and an indicator (I) to the secondary coil. The figures on the scale only serve to give a

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[1] Cathode, from *κατα* and *ὁδός*, a downward way. Anode, from *ἀνά* and *ὁδός*, an upward way. These terms, commonly applied respectively to the – and + poles of the electrical circuit, indicate the direction of the + stream to and from the battery.

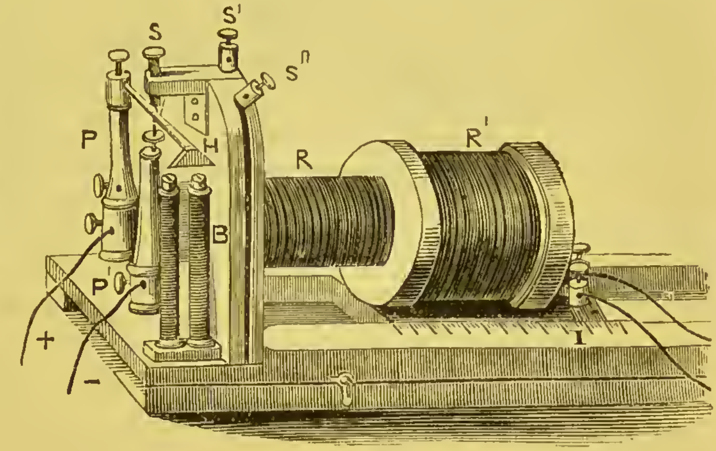

Fig. 115. Du Bois Reymond's Electromotor. (See text.)

rough approximative indication of the relative strength of the induced currents obtainable at different positions of the secondary coil, and that only when the primary current is of constant strength. The strength of the induced currents may, of course, also be varied by altering the strength of the stream in the primary spiral. In faradic machines for therapeutical purposes, the strength of the induced currents is mostly varied by partially or completely withdrawing the soft iron from the primary spiral, or by covering or uncovering it with a sheath, and thus diminishing or increasing its inducing effect.

In using the induction apparatus, the terminals of the secondary coil are joined to wires to convey the electricity to the tissues, and if a slow succession of induction shocks be desired, the wires of the voltaic cell are attached to S′ and S″, two terminals of the primary spiral. A key is interposed in the primary circuit, and an induction shock obtained when it is closed and opened. But if a rapid succession of shocks be required, an automatic key, termed a Neef's hammer (H) is employed. The wires from the voltaic cell are in that case attached to P and P′. The + wire being attached to P, the current passes to the spring carrying the hammer (H), from thence through S S′, the primary coil (R), a pair of coils (B), thence to the base of the pillar P′, and finally to the battery. The two coils (B) enclose soft iron that is rendered magnetic by the current; the hammer (H) is attracted, the spring which bears it pulled away from the point of S, and the current thereby broken; the soft iron in B loses its magnetism, and the hammer is raised by its spring; it touches S, and so closes the circuit. These changes occur very quickly, and this rapid succession of faradic shocks is commonly named the *interrupted current.*

Difference between the Closing and Opening Shocks.—If single induction shocks be sent through a muscle or nerve, it is found that the *opening* shock is the more powerful stimulus of the two. This may be readily shown by withdrawing the secondary from the primary spiral until a minimal stimulation is obtained. The difference is due to the retardation and weakening of the closing induction shock by the *extra stream* induced in the primary coil itself by the action of every single coil upon all the others. The induced extra stream is opposed in direction to the primary stream, and so retards and weakens its effect on the secondary coil. On the other hand, the intensity of the opening shock is greater and its maximum intensity instantly attained, because in the *opened* primary spiral the development of an extra stream is impossible. Thus in Fig. 117, *p* and *i* respectively represent the abscissæ of the primary and induced currents; *pc* is the curve of the primary, and *ic* that of the induction current at closure; *po* indicates the sudden disappearance of the primary current at opening, and *io* the induction shock to which it gives rise. (*The height or depth of any points of the curves from the abscissal lines indicates the intensity of the electrical stream, and the length of the abscissal lines covered by the curves—its duration. The lines o are ordinates.*) Consequently when the interrupted current is employed, the effect of the opening shocks predominates, and there is consequently a tendency to unipolar action, although there is a continual reversal of the poles. This is of no particular moment in electro-therapeutics, but in physiological experiments it is sometimes necessary to prevent it.

The closing and opening shocks may be equalised by an arrangement devised by Helmholtz (Fig. 116). A wire (V) is interposed between A and S′, and S′ is elevated until the spring of Neef's hammer cannot touch it. The screw S is elevated until the spring touches it at every vibration. The current enters the pillar P, and the whole of it at first passes through Helmholtz's wire (V), the primary coil (R), and the electromagnet (B); but the moment this is magnetised, the hammer (H) is attracted, and its spring brought into contact with S. The contact completes a shorter circuit than that of the primary coil, and so most of the current immediately returns to the battery. The closure of the shorter circuit so weakens the stream in the electromagnet that the hammer flies up and long-circuits the current, and so on. With this arrangement the current in the primary coil (R) never ceases. The "*opening*" induction shock now results merely from *weakening* of the primary current. An extra stream is now developed in the primary coil at "opening" as well as at "closure," so that the opening induction shock is retarded, weakened, and assimilated to the closing induction shock, which is also weakened. Thus in Fig. 117 the dotted lines indicate the closure (*pc′*) and opening (*po′*) of the primary current, and *ic′*, *io′*, the closing and opening induction shocks when Helmholtz's wire is used. But with the arrangement indicated in Fig. 116, the opening is still somewhat stronger than the closing induction shock; they may, however, be made exactly equal by placing a rheostat in the short circuit to augment its resistance to the electricity, and thus to increase the stream flowing in the primary spiral when the short circuit is closed. The extra stream induced in the primary coil at opening is increased, and the opening shock in the secondary spiral still more retarded, and its irritating effect therefore lessened.

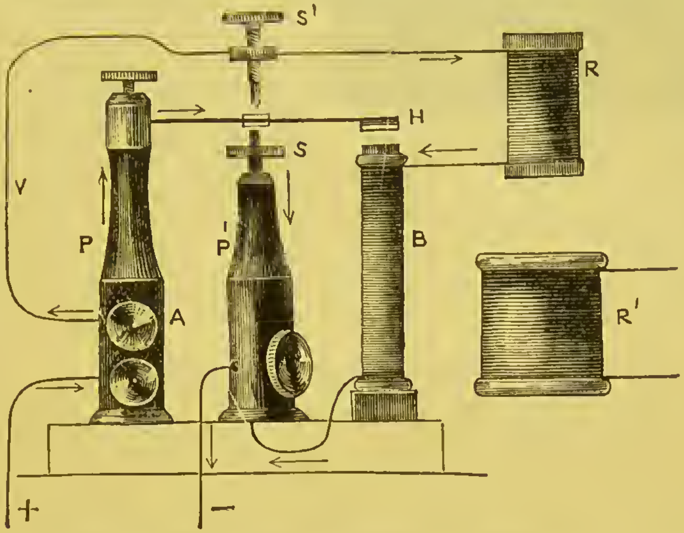

Fig. 116.—Diagram to illustrate Helmholtz's modification of the Du Bois Electromotor. (After Eckhard, slightly altered. See text.)

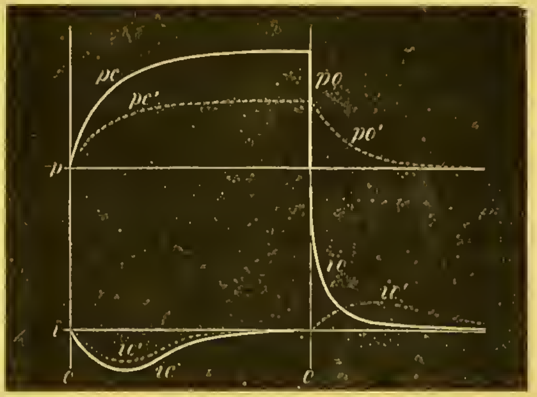

Fig. 117. To illustrate the relation of closing and opening induction shocks to primary current; *o o* are ordinates *p i* are abscissæ. (See text. After Helmholtz.)

The Extra Stream.—We have seen that on closing the primary circuit, and also on opening it, when Helmholtz's wire is used, there is a current, named the *extra stream*, induced in the primary spiral. This current is sometimes used as a stimulus for therapeutical purposes. Fig. 118 will serve to explain the manner in which it is transmitted to the tissues. Let *v* be a voltaic cell ; *p*, the primary spiral ; *m*, the electromagnet ; *n*, the point at which the circuit is closed and opened by Neef's hammer ; and *c c'*, electrodes to be applied to the tissues. The voltaic stream from *v* divides into two branches, a long branch with high resistance through the tissues from *c* to *c'*, and a short one with low resistance through the spring of Neef's hammer. When the hammer opens the short circuit at *n*, the voltaic stream is entirely long-circuited—through *c* and *c'*; but as it suddenly encounters the comparatively high resistance of the tissues it is instantly so weakened that an extra stream is induced in the primary spiral, just as happens when Helmholtz's wire is used, as already described.

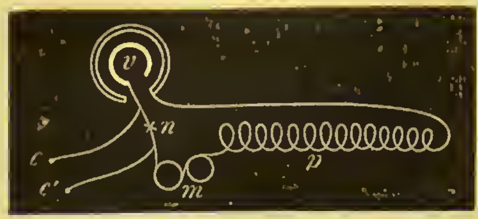

Fig. 118. Arrangement of the primary circuit when the extra stream is used as a stimulus. (Brücke.)

The extra stream may be derived from the Du Bois machine by attaching the wires from the voltaic cell to P and P', and the wires for the extra stream to S' and S". In therapeutics the extra stream is sometimes employed for the stimulation of paralysed muscles.

The instantaneous currents of induced electricity have a more powerfully stimulating effect on *nerve tissue* than the comparatively sluggish galvanic stream ; but in a muscle whose nerves have been paralysed *the faradic current may entirely fail as a stimulus, although the galvanic stream remains efficient.* When the motor nerves are paralysed by curara, faradic electricity can still excite the muscular fibres ; but its intensity requires to be increased (from 7 to 18 times, Brücke) to produce the same effect as in a non-curarised muscle. But in cases of motor nervous paralysis of considerable standing, faradic electricity may entirely fail to stimulate the muscles, probably because the contractile substance has become more sluggish in its response to stimuli, so that those of very short duration fail to affect it. Non-striped muscle is more sluggish of movement than the skeletal muscles, and probably on that account is more affected by the galvanic than the faradic current.

3. Chemical Stimulation.—It is convenient here to compare the chemical stimulation of nerve with that of muscle. The physiological limb (Fig. 1) is suitable for the former, while for the latter the sartorius of the frog should be carefully isolated, divided, and suspended by a clamp, as recommended by Kühne (Fig. 119). The effects of fluids on the muscle are tested by placing a drop on a slab with a greased surface—to render the drop convex—and then bringing the cut ends of the muscular fibres in contact with it. Substances which really stimulate the muscle cause not merely a local contraction, but one or more contraction-waves throughout the whole length of the muscle.

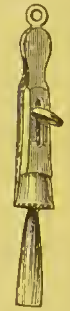

Fig. 119. Sartorius muscle of frog suspended by Kronecker's clamp, for experiments on chemical stimulation.

There are fluids, such as blood, lymph, and serum, which are entirely *indifferent*, that is, they neither excite nor injure the muscular tissue. To this category also belong fluids, such as quicksilver and oil (if its reaction be neutral), which do not mix with the juice of the muscle, and which therefore have no chemical influence. A 0·6 per cent solution of sodium chloride is of all artificial indifferent fluids the best (Nasse). But it is not perfectly indifferent, for although it does not excite the tissue it exerts a slow but certain deleterious influence. Nevertheless, it is of such service in observations on the tissues generally, that it has been proposed to name it "*physiological water*." Distilled water is a powerful irritant of muscle when injected into the vessels; the muscles pass into a state of spasm; but when applied to the surface, it has little effect.

If the nerve of the physiological limb be exposed to the vapour of ammonia, it is quickly killed without being excited. On the other hand, if the sartorius be exposed to the vapour, it contracts, showing that it is possible to stimulate muscular fibres by an agent which does not excite their nerves. The converse of this is also true; concentrated glycerin and creosote stimulate nerve, while they fail to stimulate muscle whose nerves have been paralysed by curara.

Many substances stimulate both muscle and nerve; thus potassium or sodium hydrate stimulates and kills both muscle and nerve even when very dilute (1 per mille). Neutral alkaline salts are less injurious. In somewhat concentrated solutions they stimulate both muscle and nerve, but for the latter their solutions require to be stronger. Mineral acids stimulate both muscle and nerve, but for nerve they require to be more concentrated; thus muscle is excited by a 1 to 5 per mille dilution of hydrochloric acid, while nerve requires a strength of 11 per cent. Nearly all acids kill muscle unless they be excessively dilute. We are indebted to Kühne for most of the above facts regarding chemical stimuli (*Op.* 30).

4. THERMAL STIMULATION.—A heated wire applied to a muscle excites it, unless the heat be so great that the muscle is instantly killed. If a frog's muscle be immersed in an indifferent fluid (0·6 per cent NaCl) and heated, the muscle contracts when the temperature reaches 37° C. (98·5° F.) If the muscle be quickly removed from the fluid it relaxes, but if the heat be raised to 40° C. (104° F.), and the muscle exposed to this temperature for about a minute, *heat-stiffening* ensues, and the muscle dies. On the other hand, the sudden *withdrawal of heat* by the application of a very cold body also excites muscle. But if the muscle be frozen, it is nearly always killed.

5. MECHANICAL STIMULATION.—A muscle may be stimulated by a cut or a blow, by sudden extension or torsion. These stimuli are efficient although the motor nerves be curarised. A mechanical stimulus powerful enough to stimulate a muscle usually kills the spot to which it is immediately applied.

THE DIRECT EXCITEMENT OF MUSCLE BY NON-NERVOUS STIMULI.—That the contractile substance of muscle is capable of excitement by non-nervous stimuli might be anticipated from the effects of electricity and heat on amœboid protoplasm (p. 24). It is, however, directly proved by the following facts:—1. As above stated, the vapour of ammonia stimulates muscle, while it fails to excite a nerve trunk. 2. When the nerves of a limb are paralysed, say by division, the peripheral part of the nerve loses its excitability from the point of section outwards in about four days, and becomes degenerated. Although the muscles atrophy, they can be stimulated to contraction by electricity for weeks after the nerve trunk has ceased to be excitable (Reid). 3. A muscle can be excited to contraction after its motor nerves have been paralysed by curara.

The action of curara is so important, that the manner in which some of its effects are ascertained must be considered in detail. Curara, woorara, urari, or the Indian arrow poison, are different names for a powerful toxic agent obtained from South America. Although its exact composition is unknown, it appears to be a mixture of various ingredients of a vegetable nature. Its toxic power varies in different samples. An active principle, *curaria*, has been isolated, but an aqueous solution of the crude drug is commonly used.

When a solution of curara is injected under the skin, it either enters the blood-vessels directly or through the lymphatics. It is quickly carried by the circulation to every part of the body, and passes through the capillary walls into all the tissues. On many of these it exerts no appreciable influence, but certain parts of the nervous system are, however, powerfully affected.

If two or three milligrammes of the poison be injected under the skin of a frog, paralysis of the skeletal muscles, first those of the limbs then those of the trunk, quickly supervenes, in consequence of which the animal soon lies flat on the table, and the respiratory movements of the throat cease. If the animal be stunned, the skin removed, the sciatic nerves isolated and faradised, *no muscular movement follows, but when the stimulus is applied to the muscles they contract ;* proving that the motor paralysis is *not muscular* but *nervous.* A dose which is just sufficient to paralyse the voluntary motor nerves, leaves the motor nerves of the blood-vessels intact, but with large doses they are also paralysed.

The peripheral terminations of the motor nerves are the parts first affected. This is proved as follows :—The sciatic artery of one leg (Fig. 120, A) of a frog is tied at the upper part of the limb (*a*). The curara is then injected under the skin of the trunk, and it is carried to every part save leg (A) below the seat of ligature. When the palsy has supervened, it is observed that *the unpoisoned leg is drawn up,* while the other is quite flaccid. *The animal can move the unpoisoned limb, although the poison has freely circulated through the lumbar part of the nerves of that limb,* showing that the trunk of the nerve is not paralysed.

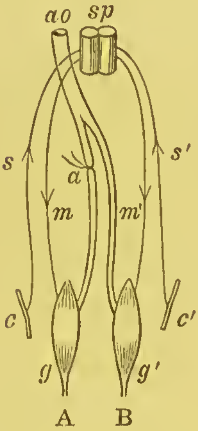

Fig. 120. Scheme of certain tissues in the hind legs (A B) of a frog, to explain the curara experiment. *sp*, Spinal cord ; *m m'*, motor, *s s'*, sensory nerves ; *g g'*, gastrocnemii ; *c c'*, skin ; *a*, seat of a ligature on sciatic artery.

If in the performance of experiments in the above manner with agents which paralyse nerves, it be found that *motion does not follow direct excitement of the nerve in the lumbar region, no conclusion must be arrived at regarding the seat of palsy until another experiment has been performed.* In this, *after tying the sciatic artery,* a ligature is passed *under* the sciatic nerve and firmly tied round the limb. All the structures save the nerve are thus constricted, *so that the blood cannot find a collateral path down the limb.* If after the poison has acted, stimulation of the nerve in the lumbar region give rise to no motion, while stimulation of the nerve beyond the seat of ligature does, it is certain that the poison paralyses the nerve trunk. Care, however, must be taken that the nerve is not dragged upon at the seat of ligature, otherwise it will be paralysed (Bernard, *Op.* 85).

Since the poison does not paralyse the sciatic nerve in the lumbar region, it might be safely inferred that the lower part of the nerve trunk also escapes. Nevertheless, this may be proved as follows :—The gastrocnemius of a frog (which may be pithed) is denuded, the tendo achillis cut across, the muscle stripped from subjacent parts, and its upper bony attachments divided, care being taken not to injure the nerve. A ligature is passed under the nerve close to the gastrocnemius, and tied firmly around all the structures of the limb save the nerve, to prevent bleeding. The poison is then administered as before, and although it can circulate in the sciatic nerve close to the gastrocnemius, it is not paralysed, for when exposed and stimulated the gastrocnemius contracts. *Therefore, in the unligatured limb the palsy of the motor nerves must be intramuscular.* If the fibres of the sciatic nerve are not paralysed, it is not likely that similar nerve-fibres within the muscle are paralysed.

Reasons for believing that the *terminations* of the motor nerves are paralysed may be obtained as follows :—The sciatic artery of one limb of a frog is ligatured, and the animal poisoned with curara as above described. Both legs are then prepared as physiological limbs with the nerves as long as possible. Both femora are fixed in a clamp (Fig. 121) suitably supported, the legs being so placed that the gastrocnemii are uppermost. The toes are allowed to hang down, and straws are attached to serve as delicate indices of movement. The nerves (*n*) are laid on electrodes connected with a commutator (C). Two very thin wires are attached to C, and the free end of each is thrust through the gastrocnemius close to its tendon. The commutator is then joined by a pair of long thin wires to the secondary coil of the Du Bois electromotor (Fig. 115). The bridge of the commutator (Fig. 121, H) is arranged to send the current through the nerve. The secondary coil of the electromotor is pushed near to the primary, and the nerves stimulated. *Only the muscle of the ligatured limb contracts.* The bridge of the commutator is then turned, and the current sent through the muscles. *Both muscles contract.* Both facts have been previously stated, but they are here repeated because of the clearness of the method of demonstration. The secondary is now pulled away from the primary spiral, and as the current becomes weaker and weaker, a point is reached where the *poisoned muscle passes into a state of rest, while the unpoisoned muscle remains contracted.* When the current is still further weakened, of

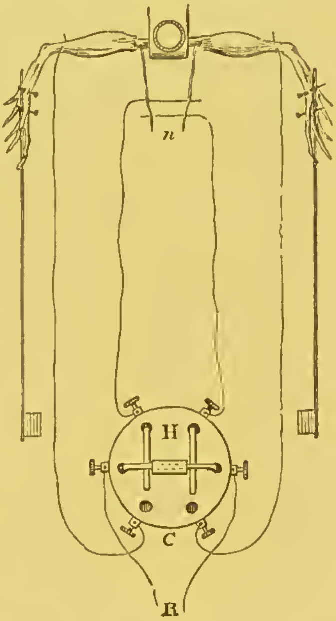

Fig. 121. The curara experiment (see text). *n*, Nerves ; H, handle of commutator (C) ; R, wires joined to faradic machine.

course the latter also ceases to be excited; proving that in the poisoned muscle the excitability to faradic electricity is diminished. As this result cannot be attributed to a toxic effect on the muscular fibres, *for curara in however large a dose never paralyses them, it must be ascribed to a paralysis of the very terminations of the motor nerves* (Rosenthal).

It may be inferred from the above that nerve is more excitable by faradic electricity than muscle (see p. 148); so that when a *minimal* but efficient faradic stimulus is applied to a normal muscle it *directly* excites its *nerves only,* and the current requires to be stronger to directly stimulate the muscular fibres.

Curara paralysis is not, however, entirely confined to motor nerves; the spinal cord is also affected. If a frog be pithed and its brain destroyed, reflex actions of a definitely localised character may be readily induced by applying a piece of bibulous paper dipped in vinegar to any part of the cutaneous surface of the trunk or legs. The nervous impulse travels from the skin (Fig. 120, *c*), through the sensory nerve (*s*), to the spinal cord (*sp*), and is transmitted by its nerve cells in various directions through motor nerves (*m*) to muscles. The action is reflex, and implies neither sensation nor volition, yet the toes are exactly directed to the seat of the irritation. Ligature of one sciatic artery does not for a very considerable time affect the reflex manifestations even in the bloodless leg. If the animal be now curarised by injecting the poison under the skin of the trunk, it is found after leg B (Fig. 120) is paralysed, that application of vinegar paper, say to the thigh of that leg, induces reflex movements of leg A, proving that the *sensory nerves* of B are not paralysed. The reflex movements are at first normal, but when the spinal cord becomes affected by the poison they lose their normal purpose-like character, and become quite indefinite and disordered, showing that the spinal cord is really affected. Eventually, no reflex action can be induced, although the motor nerve trunk of leg A remains excitable above the seat of ligature. The negative result is doubtless owing to paralysis of the spinal cord, because of the change in the character of the reflex action which precedes its total disappearance.

Cases of curara poisoning in the human subject have shown that if artificial respiration be efficiently maintained the poison produces no painful sensations. On the contrary, it induces a state of somnolence (Voisin, *Op.* 84, x. 578). As the spinal cord of the frog is paralysed by large doses of the poison, it is probable that the spinal cord of mammals is similarly affected.

THE CONTRACTION OF MUSCLE.

For an accurate study of muscular contraction it is necessary to register the movement with the aid of a myograph. The various forms of this instrument consist of a lever moved by the *shortening* or by the *thickening* of the contracting muscle. The movement is recorded upon smoked paper or glass.

PFLÜGER'S MYOGRAPH has been already referred to (Fig. 111). The end of the lever bearing the writing style is placed at right angles to the smoked plate, and as the latter is motionless when the muscle contracts, a vertical line—an *ordinate*—indicating the *degree* of contraction is traced on the blackened surface (Fig. 111). If the plate be drawn across the style during the contraction, a *curve* is obtained, indicating not merely the *degree* but also the *duration* of the contraction. This instrument, however, is not intended for observations on the time of contraction.

METHOD OF RECORDING TIME ON A MOVING SURFACE.—For the measurement of the duration of a muscular contraction, the rate at which the recording surface moves during the contraction must be known. The simplest and most accurate method is to synchronously register the vibrations of a tuning fork immediately below the writing point of the myographic lever. The fork may be thrown into vibration by striking or nipping it, but it is more convenient to keep its vibrations of uniform amplitude by driving it with electricity (Fig. 122). Its vibrations may be directly recorded on the blackened surface by a pointed strip of brass or aluminium fixed to one of its limbs (*b*); but as it is often difficult to support a tuning fork in suitable proximity to the recording surface, its vibrations may be conveniently transferred to the chronograph of Deprès (*c*), and registered by it. This valuable instrument is a small electromagnet with an armature bearing a writing style, and capable of oscillating synchronously with a tuning fork. The armature is held by a fine elastic band at a little distance from the electromagnet, and the same electrical stream which drives the tuning fork, and which is interrupted at every vibration, also drives the chronograph by interruptedly magnetising its iron core, and thus causing an oscillating movement of its

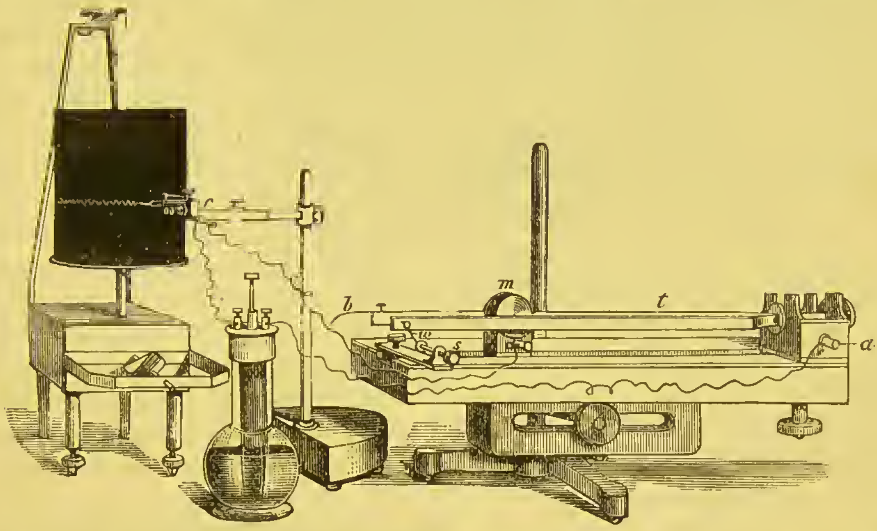

Fig. 122. The chronograph of Deprès (*c*) arranged to record the vibrations of a tuning fork (*t*). The fork and chronograph are driven by electricity. The current enters—say at *a*, traverses the fork, a platinum wire (*w*), an adjustable platinum contact (*s*), and an electromagnet (*m*); it then passes to the electromagnet of the chronograph (*c*), and back to the voltaic cell. By the magnetisation of *m* the limbs of the fork are attracted, and the circuit thereby broken at the platinum contact (*w*). By this, *m* is demagnetised, and the elasticity of the fork restoring its limbs to their former position, the circuit is again closed at *w*. The magnetic changes in the chronograph (*c*) occasion vibrations of its writing style synchronous with those of the fork. *b* is a style for directly recording the fork's vibrations when desirable.

armature and style. The Deprès chronograph is capable of recording vibrations at all speeds up to 700 or 800 per second, and is therefore of great service.

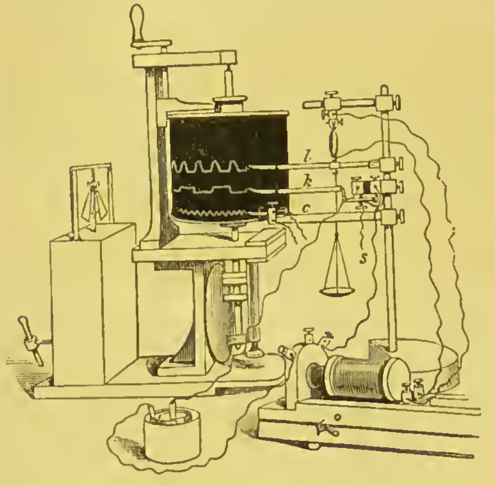

Fig. 123. Marey's myographic lever (*l*). *k*, Key, with marking lever; *s*, string for opening key; *c*, chronograph. The key is in the primary circuit of a faradic machine, and wires from the secondary circuit pass to the muscle.

THE CONTRACTION CURVE OF A FROG'S MUSCLE may be obtained with the myographs of Marey and Fick. In *Marey's myograph* a frog's gastrocnemius is hooked to a *light* lever (Fig. 123, *l*), with aluminium foil, or a bristle for a writing style. When desirable, a pan for weights is hooked to the lever. An electrical key with a marking lever (*k*) is placed below the myograph, and beneath this again there is a chronograph (*c*). The three writing points are placed on the same vertical line on the recording surface. The electrical arrangements in Fig. 123 are intended for stimulation of the muscle with single faradic shocks, by opening and closing the key which, for that object, is placed in the primary circuit. In Fig. 124 there are two curves (*c c′*), respectively produced by a weak opening and a weak closing faradic shock transmitted through a curarised muscle; *c′* is lower than *c*, because the closing is a feebler stimulus than the opening shock. Fig. 125 shows two similar curves obtained from *the same muscle* by slightly increasing the strength of the stimulus. In each case, the curve is that of a single contraction.

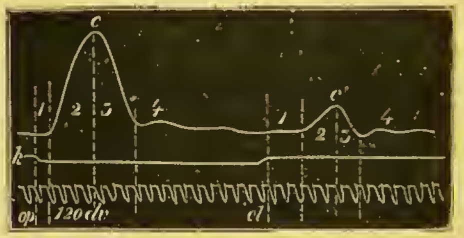

Fig. 124. *c*, Curve of a single contraction of a curarised frog's gastrocnemius induced by a weak opening shock directly applied at *op*; *c′*, curve of contraction induced by a closing shock applied at *cl* (one small Grove's cell; second coil of the Du Bois electromotor at 166 M.M. from first coil); *k*, marking lever line; 120 *d v*, 120 double vibrations of diapason per sec.; 1, 2, 3, and 4 indicate the events following the application of the stimulus.

The myograph used in the above experiment does not give the true curve of contraction, because the relation of the writing point to the cylinder is such that, with the cylinder *at rest*, the lever, when lifted, describes an arc (Fig. 125, *l*). This curve *proper to the lever* is added to the true curve of contraction, and requires to be eliminated from it. This is done by projecting an ordinate (Fig. 125, *o*) from the point where *l* springs from the abscissa. A series of abscissæ (*a*) are then drawn from the ordinate through the lever curve and muscle curve, and the points of the latter are shifted to the left to the same distance as that between the lever curve and ordinate on the corresponding abscissæ. *The correction of* *such curves is always important when the duration of their constituent parts is to be measured.*

Four events follow the application of a stimulus to a muscle; 1, a period of latent stimulation; 2, a period of contraction; 3, a period of rapid relaxation; 4, a period of slow relaxation. The 2d, 3d, and 4th events constitute the muscle curve.

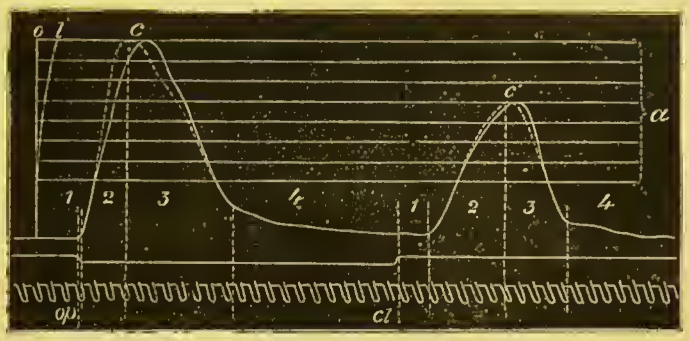

Fig. 125. Two single contractions produced by a more powerful stimulus than in Fig. 124 (second coil at 160 M.M. from first coil) applied to the same muscle. *o*, Ordinate; *l*, curve traced by lever, with cylinder at rest. The *dotted* curve under *c* is the true curve of contraction obtained by eliminating the lever curve (*l*); *a*, abscissæ drawn to facilitate the elimination of the lever curve. The other letters and numbers indicate the same as in Fig. 124.

1. *The Latent Period.*—The faradic shock is instantaneously transmitted to the muscle when the marking lever key is opened or closed. A brief interval—*the period of latent stimulation*—elapses between the application of the stimulus and the resulting contraction. The latent period varies with the strength of the stimulus; thus it is shorter after an *opening* than after a *closing* induction shock (Fig. 124), and when both shocks are intensified the latent period is shortened in both cases (Fig. 125). It also varies with the excitability of the tissue, being lengthened when the excitability is lowered. It is measured by intersecting the chronogram with a pair of vertical lines, enclosing the interval between the application of the stimulus and the beginning of the contraction. In *c'*, Fig. 124, its length is $\frac{2.5}{120}$ ($\frac{1}{48}$) sec.; in *c'*, Fig. 125, it is $\frac{2}{120}$ ($\frac{1}{60}$) sec.; in *c*, Fig. 124, it is $\frac{1}{120}$ sec.; while in *c*, Fig. 125, it is $\frac{0.3}{120}$ ($\frac{1}{400}$) sec. Therefore, in the same curarised muscle the latent period may vary from about $\frac{1}{60}$ to $\frac{1}{400}$ of a second, according to the strength of the stimulus. With very powerful stimuli it is almost instantaneous. In human voluntary muscle its duration is $\frac{1}{80}$ sec., with a moderate opening induction shock directly applied. In measuring the latent period it is essential that the lever be unloaded, otherwise it is not moved until a little time after the discharge of mechanical energy has really begun, and has become sufficiently intense to move the heavy lever; the latent period would in such case appear longer than it really is.

Although there is no visible motion during the latent period, it can be proved with the differential rheotome and galvanometer, that the molecules of the sarcous substance are thrown into a state of electrical disturbance, commonly termed the *negative variation* of the muscle current. This electrical disturbance in no way depends on the nature of the stimulus. It occupies the latent period, and is over before the contraction begins (Bernstein).

2. *The contraction* is the second event following the stimulation of the muscle, and results from the transformation of chemical into mechanical

energy. Its duration varies with the intensity of the stimulus, as may be seen in Figs. 124 and 125, where, as shown in the following table, the contractions produced by different stimuli vary from $\frac{1}{52}$ to $\frac{1}{17}$ sec. in the same frog's muscle curarised. The duration of the contraction also varies with the excitability of the muscle. In human voluntary muscle with a moderate stimulus, its duration is about $\frac{1}{27}$ sec.

	Closing Induction Shock.		Opening Induction Shock.	
	Contraction.	Rapid Relaxation.	Contraction.	Rapid Relaxation.
Weak Stimulus (Fig. 124).	$\frac{2 \cdot 3}{120} = \frac{1}{52}$ sec.	$\frac{2}{120} = \frac{1}{60}$ sec.	$\frac{3 \cdot 5}{120} = \frac{1}{34}$ sec.	$\frac{3}{120} = \frac{1}{40}$ sec.
Rather Stronger Stimulus (Fig. 125).	$\frac{5}{120} = \frac{1}{24}$ sec.	$\frac{3 \cdot 6}{120} = \frac{1}{33}$ sec.	$\frac{3}{120} = \frac{1}{40}$ sec.	$\frac{7}{120} = \frac{1}{17}$ sec.

3. *The rapid relaxation* of the muscle which immediately follows its contraction is primarily due to the elastic recoil of the muscle. Its duration varies considerably in the same muscle, as shown in the preceding table. It varies with the intensity of the preceding contraction; thus, with a weak stimulus, it is *shorter* than the contraction, but with a stimulus of considerable strength it is *longer* (Fig. 125 *c*); the more intense the preceding contraction, the more slowly does the muscle relax. The elastic recoil is feeble, and may therefore be prevented by even slight resistance. If a weight be applied to the muscle, the relaxation is hastened by the stretching force.

4. *The slow relaxation* of the muscle has been named by Hermann *the residual contraction*, or *contraction remainder*. It varies greatly,—being longest when the contraction is most intense, and when the stretching *force* is feeblest. After a powerful stimulation of an excised muscle, it may, owing to arrested nutrition, become permanent. The tardy return of the muscle to its former length is by some ascribed to *elastic after-action* (see p. 141), but the fact that although a heavy lever may for a moment at once stretch the muscle to its full length, it is drawn up again by the residual contraction (Fig. 128, *n*), throws doubt on this.

The curve of contraction with the Pendulum Myograph.—The pendulum myograph was invented by Fick for measuring the velocity of nerve-energy, and for the study of muscular contraction. It is a pendulum (Fig. 126) with a pair of glass plates at its swinging end. One of the plates (A) is smoked, and serves to record the muscular contraction. The other (A′) is merely a compensator; thus when A is lowered by the screw (S), A′ is elevated to the same extent, so that the period of the pendulum's oscillation is kept constant. The pendulum is drawn to one side, and held there by a catch placed in suitable relation to a strong projecting tooth (B). When the pendulum is liberated from the catch it oscillates, and at the end of its swing is caught and held by another catch suitably placed. It is convenient to have the pair of catches screwed to an arc (Fig. 127), so that the interval between them may be varied, and any desirable velocity of the recording surface obtained. The lever to which the frog's muscle is hooked may be the heavy German lever (Fig. 126) or the light lever of Marey. The latter is preferable when the curve of contraction is desired, for although the heavy lever be counterpoised, the momentum it acquires—being propor-

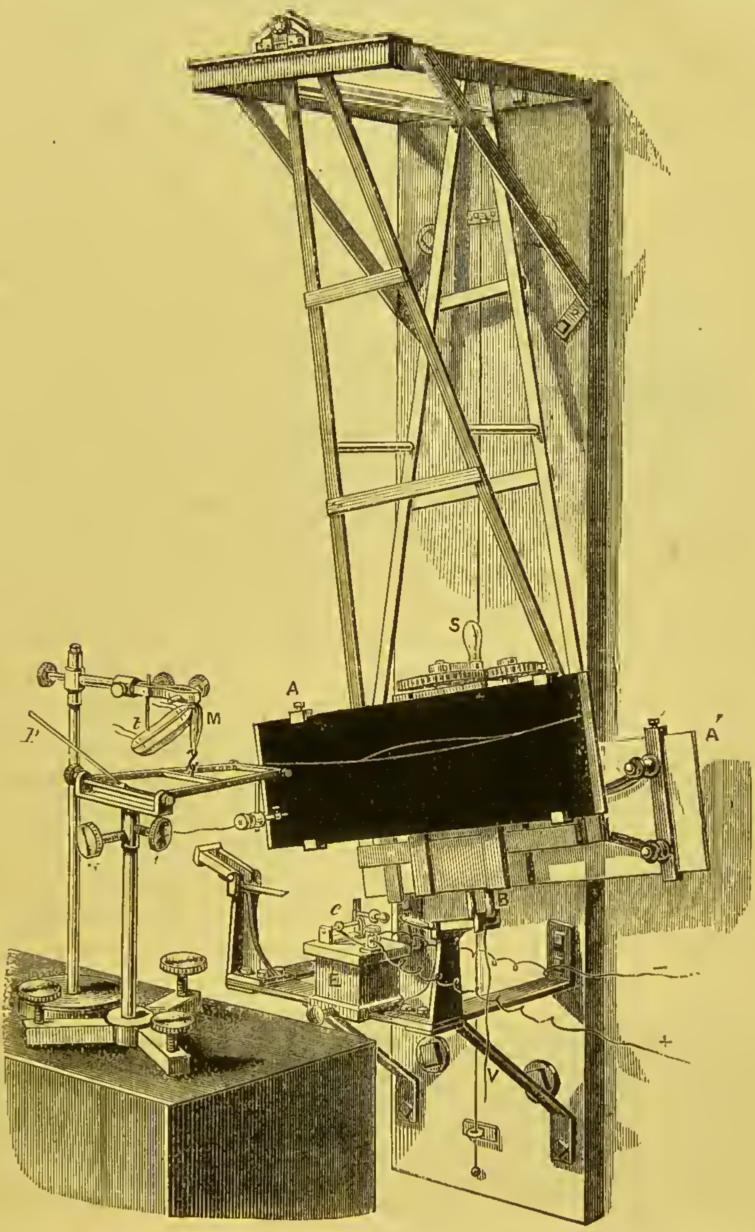

Fig. 126. The pendulum myograph. A A′, Glass plates clamped to the pendulum; S, screw for elevating or lowering the plates; M, muscle attached to lever; *p*, rod for moving the lever with the hand in the experiment on the velocity of energy in human sensory nerves. The trough (*t*), with double pair of wires, is used in the experiment on the velocity of energy in the motor nerve of the frog. B, tooth by which the pendulum is caught and held before and after its swing; *v*, cord for depressing the catch. E, support for electrical key (*e*).

tional to its mass—is so great that secondary oscillations are introduced, and complicate the muscle curve; thus the momentum acquired during the descent of the lever carries it for a moment to the abscissa (Fig. 128), or even below it, whereas a light lever does not in its descent reach the abscissa until the residual contraction is over. But if Marey's lever be weighted, secondary oscillations are thrown into the muscle curve.

Time is recorded on the plate by a Deprès chronograph (Fig. 127, *c*), the writing point of which is placed exactly below that of the myographic lever. A pair of wires pass from the secondary coil (*s*) of an induction machine to the muscle, and a key (*k*) is placed in the primary circuit (*p*). When the pendulum is allowed to swing, its tooth opens the key, and the single contraction, induced by the induction shock, is registered on the smoked plate before its single oscillation is ended. The chronograph is drawn aside, the key is left open, and the pendulum is allowed to swing again with the muscle at rest, to obtain an abscissa (Fig. 127, *a*). The pendulum is then reset as at first, and after the key is closed the pendulum is very carefully moved until it just opens the key, and no more. Being held at rest while the key is just opened, the contraction of the muscle causes the lever to trace a vertical line (*s*), indicating the point of the abscissa at which the stimulus is applied to the muscle. The latent period (between *s* and *s′*) is exaggerated in Fig. 128 by the circumstance that the lever used in that experiment was heavy, and therefore not set in motion until some little time after the contraction had begun. As the lever used in Fig. 128 moved at right angles to the recording surface (see Fig. 126), no correction of the curve is needed (see p. 154).

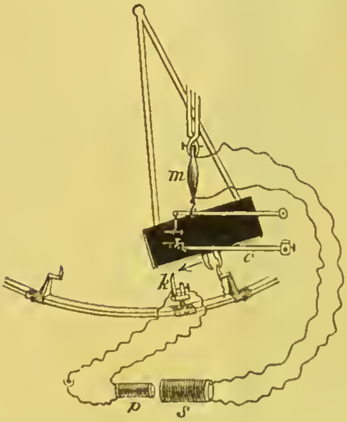

Fig. 127. Arrangement of the pendulum myograph for obtaining the curve of muscular contraction. *m*, Muscle; *p* and *s*, primary and secondary coils of induction machine; *k*, key; *c*, chronograph of Deprès.

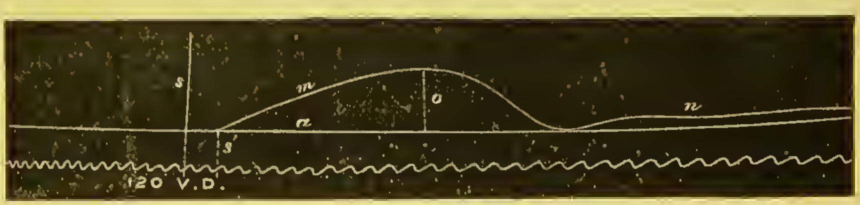

Fig. 128. *m*, Single contraction of frog's gastrocnemius traced on the pendulum myograph with a heavy lever; *s*, point at which the stimulus was applied to the muscle; *s′*, the commencement, and o, the end of the act of shortening; *n*, the slow relaxation.

THE CONTRACTION CURVE OF HUMAN MUSCLE may be obtained by registering the *thickening* of the adductor muscle of the thumb with Marey's myographic forceps (Fig. 129). Attached to one limb of the forceps there is a tambour covered with vulcanised caoutchouc membrane with an aluminium plate in its centre, against which the other limb of the forceps presses. An elastic band around the forceps causes them to nip the muscle. When the muscle contracts and widens the forceps, air is pressed from the tambour (*m*) into the second tambour (*t*), on the membrane of which there rests a lever for recording the muscular movement. Single contractions are obtained by transmitting single induction shocks through the muscle. Fig. 130 shows a curve of a single contraction of the adductor of the thumb taken on the pendulum myograph with the above arrangement. The stimulus was an opening induction shock of moderate intensity sent through the muscle at *s*. The curve of contraction is similar to that of the frog's muscle when registered by a light lever. In this experiment the latent period was $\frac{1}{80}$ sec., and the duration of the contraction (the second event) $\frac{1}{27}$ sec., but doubtless both periods vary with the strength of the stimulus, as in the frog's muscle.

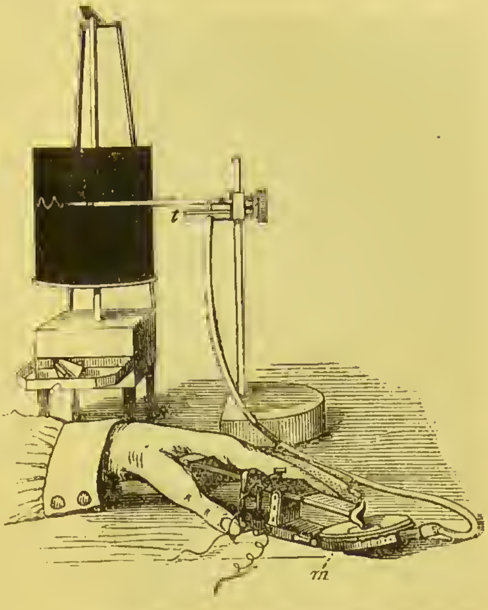

Fig. 129. Marey's myographic forceps applied to adductor of thumb; *m*, tambour of the forceps; *t*, tambour with recording lever.

The duration of a single contraction varies much in different muscles of the same animal, and in different animals; thus it is shortest in the striped skeletal muscles (about $\frac{1}{25}$ sec.), about eight times as long in the striped muscle of the heart, and still longer in non-striped muscle. It is nearly twice as long in the *red* as compared with the *pale* muscles of the rabbit (see p. 132) (Ranvier, *Op.* 11, 1874, p. 5). It is about five times longer in the hyoglossus than in the gastrocnemius of the frog (Marey, *Op.* 74, p. 364). It is shortest in insects and longest in the tortoise (Marey, *Op. cit.*) As regards rapidity of contraction, the ordinary striped muscle of different animals may be arranged in the following order, beginning with the slowest:—the tortoise and hybernating mammals, the frog, mammals, fishes, birds, insects (Marey, *Op. cit.*)

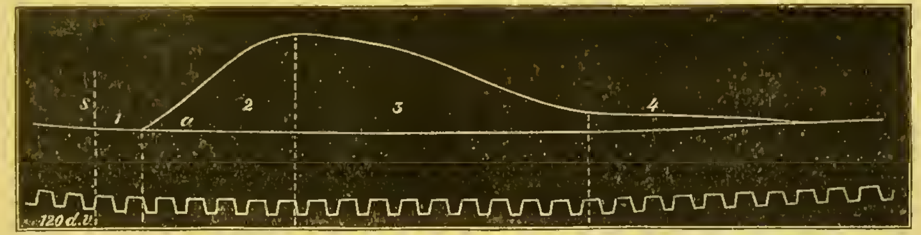

Fig. 130.—Single contraction of human voluntary muscle induced by an opening induction shock sent through the muscle at *s*. 1, 2, 3, 4 are the events that follow the stimulation before referred to; *a*, abscissa.

The duration of contraction is lengthened by fatigue, and especially by cold. The difficulty in executing delicate movements when the hands and arms are chilled is probably due to the direct influence of the cold on the muscles.

TETANUS.—Muscular contraction may be simple or compound; a *simple* is a single contraction, a *compound* contraction is a succession of single contractions. When faradic shocks are applied to a muscle or its nerve in quick succession, the relaxation of the muscle becomes incomplete (Fig. 131), and if the stimuli be sufficiently rapid the single contractions become so completely fused together that the myograph traces a line as if the contraction were simple. This apparently simple, but in reality compound, contraction is named Physiological Tetanus (Fig. 132). The rapidity of stimulation required to produce the continuous curve of complete tetanus varies in different muscles according to the duration of a single contraction of the muscle. Thus, complete tetanus is produced in the sluggish muscle of the tortoise by two stimuli per second, in the hyoglossus of the frog by 10 per second, while in the gastrocnemius of the same animal 27 stimuli per second are required (Marey, *Op.* 74). The sluggish red muscles of the rabbit require 10 stimuli per second, while the pale muscles of the same animal require from 20 to 30 per second (Kronecker and Stirling, *Op.* 2, i. p. 395).

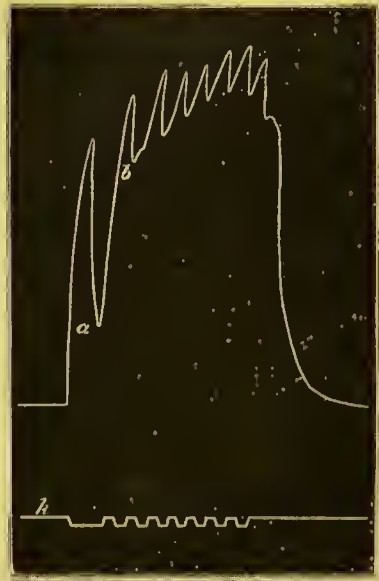

Fig. 131.—Incomplete tetanus of human muscle due to direct stimulation by single faradic shocks at the rate of about 10 per second. The greater fall of the lever between *a* and *b* is due to a longer interval between the first and second stimuli than between the others; *k*, line traced by marking lever (Fig. 123, *k*).

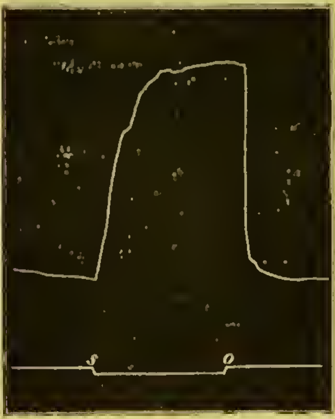

Fig. 132.—Curve of complete tetanus of human muscle due to a very rapid succession of faradic shocks, beginning at *s* and ending at *o*.

THE SOUND OF A TETANISED MUSCLE.—When the ear is applied, with the aid of a solid stethoscope, to the muscles of a rabbit recently killed, and tetanised by the interrupted current, a rumbling musical note—the *muscular sound*—is heard. The pitch of the note varies with the rapidity of succession of the stimuli; each stimulus producing a vibration in the sarcous matter from the rhythmical succession of which the musical note results. The muscular sound may be readily heard if the jaws be clenched during the night when all extraneous sounds are hushed. The pitch of the note produced by a voluntary contraction is 39 vibrations per second (Helmholtz). By transferring the actual vibrations of the muscle by resonance to a strip of flexible metal, Helmholtz proved that the note actually produced by the

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ERRATA IN PART I.

Page 24, first line, *for* Fig. 8 *read* Fig. 7.
Page 42, line 16 from top, *for* H *read* H_2.
Page 46, lines 27 and 29 from top, for *subtilis* read *subtile.*
Page 48, „ 17 „ 32 „ „ „
Page 49, line 31 „ „ „

APPENDIX TO PART I.

Page 93, § 3, second line.—Nerves have been recently discovered in tendon by Rollett.